Chapter 11

PROGNOSIS FOR SEIZURE CONTROL

By the end of 1959, the Michigan Epilepsy Center had files of over 1,000 patients who had been seen by a team of specialists including neurologists, psychiatrists, electroencephalographers, psychologists, pediatricians, and social workers over the previous ten years. The case records were exceedingly detailed and could form a solid basis for statistical treatment of the data. The Center is, however, a consulting facility only. It makes recommendations to the treating physician and does not engage in continued day-to-day patient management. It works through the referring physician rather than taking over patient care entirely. This can obviously affect the results of follow-up investigations. Treatment recommendations may not have been carried out to the fullest extent either by the physician in charge or by the patient, and continued medical supervision by a specialist might have improved the outcome in a number of cases. The results of the follow-up studies of patients seen at the Center therefore do not necessarily reflect what could have been accomplished under ideal circumstances, but what is actually happening in a large metropolitan area of the United States. There is no reason to believe that the level of general medical care is inferior in Detroit to that in other large cities of this country and the results can probably be taken as being representative for the country at large.

There is, of course, always the problem of patient selection. One may assume that only the most inveterate cases would be referred to a special facility as an epilepsy center, and one would therefore obtain a negative selection that would *a priori* bias the

results. This is fortunately not the case. Patients are at times referred after their very first seizure; others come because the diagnosis is in doubt; others have no particular problem in regard to seizure control but present psychiatric or intellectual difficulties as the prime handicap, and there are, of course, also some patients who have made the rounds and tried most other facilities with the Michigan Epilepsy Center being just another stop on the road in search of seizure control. For all practical purposes, the Center sees probably a rather typical cross section of patients with known or suspected epilepsy.

It became apparent that the fullest use of the detailed workup of the patients could only be made by having most of the information in a form that would allow statistical manipulation of the data. For this reason code sheets were constructed that covered the neurological history, neurological examination, psychiatric evaluation, psychological test results, laboratory examinations, and EEG findings. By the end of 1959 these sheets were ready for use with a clinical population. We simply wanted to know whether there were any features in all of the material that was so meticulously accumulated that would bear a definitive relationship to the prognosis for epileptic children in regard to the previously mentioned areas. It was also decided to proceed with the workup of the data in as unbiased a fashion as possible. There was no hypothesis that was to be confirmed or rejected. The data were handled as if we knew nothing whatsoever about epilepsy, letting the results of the statistical findings dictate the subsequent steps of data workup rather than guiding it by preconceived assumptions.

FIRST FOLLOW-UP STUDY

In order not to be confounded by temporary short-term remissions it was decided to select only those patients who had fulfilled the following criteria: (1) had been seen at the Center at least five years earlier; (2) had received the complete workup as previously stated; (3) lived in the greater Detroit metropolitan area; (4) had been ten years old or younger at the time of

initial evaluation, and (5) had received a definitive diagnosis of epilepsy.

The last consideration involved a problem of definition. Does a patient who has had only one seizure merit a final diagnosis of epilepsy, or should one require the presence of recurrent seizures for the diagnosis? In order to avoid the uncertainties of the isolated seizure in childhood, the rule was adopted that the patient must have had at least three seizures that could be diagnosed as clearly epileptic on the basis of the clinical history. Attacks of abdominal pain, headache, or syncope were excluded and so were breathholding spells and febrile convulsions. This policy led, therefore, to a definitely epileptic sample but may have excluded some patients with the mildest forms of the illness. When all the restrictions were applied, our supply of potential cases had dwindled considerably. After being unable to locate some, getting refusals to cooperate with reexaminations by others, we ended up with thirty-two patients who could be reexamined. Five (15.6%) of these had been institutionalized in the meantime at Caro State Hospital for Epileptics, and these patients were transferred for purposes of reevaluation to the Lafayette Clinic. All patients had a repeat electroencephalogram, and information in regard to seizures, behavior, and school achievement was obtained at that time. The patients were reexamined during the first half of 1960. They had been seen initially between 1950 and 1954 inclusive.

Description of Sample

The average duration of follow-up was seven years and the distribution is shown in Table 27. The mean age at initial evaluaton was 6.2 years, and the breakdown is listed in Table 28. There were nineteen boys and thirteen girls in the group. The mean duration of the illness prior to initial evaluation was 2.9

TABLE 27

FOLLOW-UP SPAN

Years	5	6	7	8	9
Patients	9	10	5	7	1

TABLE 28
AGE AT INITIAL EVALUATION

Years	1	2	3	4	5	6	7	8	9	10
Patients	2	1	1	4	7	2	2	4	3	6

years, and the distribution is detailed in Table 29. The seizure types are shown in Table 30. Nine patients had more than one seizure type. In order to avoid duplication, further description of the initial findings will be shown in relation to the follow-up results. Of the twenty-seven patients living in the community all

TABLE 29
DURATION OF ILLNESS

Years	1 or less	2	3	4	5	6	7	8	9
Patients	9	9	3	5	2	2	1	0	1

but five were still taking anticonvulsant medications (81.5%). Four of these five patients had been seizure free for five years or more; the fifth patient was still having seizures, but the mother claimed to have lost the prescription.

From the total group living in the community, fifteen (55.6%) were still having seizures; three (11.1%) had remitted for one year prior to follow-up; one (3.7%) for two years; two (7.4%) for five years; three (11.1%) for six years; two (7.4%) for eight years, and one (3.7%) for nine years.

A terminal remission of two years or more had therefore oc-

TABLE 30
SEIZURE TYPES

Major seizures with focal features	11
Major seizures without focal features	9
Psychomotor seizures	7
Minor focal motor seizures	4
Absence	4
Minor nonfocal motor seizures	3
Akinetic	2
Myoclonic jerks	1

curred in nine (33.3%) patients, and a terminal remission of five years or more in eight (29.6%) patients.

Electroencephalogram

The initial EEG had been normal in eight (25.8%); borderline in one (3.1%); mildly abnormal in two (6.3%); moderately abnormal in six (18.8%), and markedly abnormal in fourteen (43.8%). One record was technically poor and had to be disregarded. It should be pointed out that the patients were, for the most part, already on some anticonvulsant regime which was not discontinued for the test. A comparison of the initial EEG with the follow-up EEG is shown in Table 31. The EEG had stayed

TABLE 31

AMOUNT OF EEG ABNORMALITY

	Initial EEG	*Follow-up EEG*
Normal	8	10
Borderline	1	3
Mildly abnormal	2	4
Moderately abnormal	6	3
Markedly abnormal	14	10
Technically poor	1	2

the same in eight cases (25.0%); improved in eleven cases (34.4%); deteriorated in seven (21.9%). It was normal on both evaluations in three (9.4%) and three patients could not be compared because of technical difficulties. This refers to an overall evaluation of EEG abnormalities. Table 32 shows a com-

TABLE 32

SEIZURE PATTERNS

	Initial EEG	*Follow-up EEG*
No seizure patterns	9	16
Questionable	3	3
Mild	3	2
Moderate	6	4
Marked	10	5
Technically poor	1	2

parison in regard to seizure patterns in the initial and follow-up EEG. The amount of seizure patterns had remained the same in two patients; it had decreased in sixteen; increased in five; no seizure patterns had been present on either occasion in six, and no comparison was possible in three patients. In regard to focal abnormalities the results are presented in Table 33. The amount

TABLE 33

FOCAL ABNORMALITIES

	Initial EEG	*Follow-up EEG*
None	21	26
Mild	4	3
Moderate	3	0
Marked	3	1
Technically poor	1	2

of focal abnormalities had not remained the same in any of the patients; it was less in ten, more in three; focal patterns were not seen in either recording in sixteen, and no comparison was possible in three cases.

The tendency of the electroencephalogram was, therefore, towards improvement, especially in regard to the presence of seizure patterns and focal abnormalities.

Of the five patients whose seizure patterns had become worse, four were still having seizures (one state-hospitalized), and one was controlled for at least two years; however, his rating had gone only from "none" in the initial EEG to "questionable" in the follow-up EEG.

Of the three patients whose focal disturbance had become more pronounced, one was controlled (the rating went from "none" to "mild") and two were still having seizures.

Of the sixteen patients whose seizure patterns had improved, five had shown clinically a terminal remission of at least two years; the others were still having seizures. Seizure patterns which had been present in the initial EEG disappeared from the recordings in ten patients; but only three of these had clinically remitted, while the others were still having seizures.

An investigation into EEG background activity showed that

the general tendency was towards an increase in amount of alpha rhythm, decrease in theta activity, and decrease in amplitude by the time of follow-up. This agrees with what one would expect to occur as a result of maturation. The improvement of the background activity was not related to a change in the seizure state. Only two patients showed deterioration in background frequencies, both were still uncontrolled by medication although one of the two patients had shown some improvement in his seizure disorder.

The five institutionalized patients had the following seizure patterns: infantile spasms-hypsarhythmia in two, focal minor motor seizures in two, focal major seizures in one. The age at time of onset of the illness was since birth in one, seven weeks in one, eleven months in one, eighteen months in one, and two years in one.

Seizures had started before the age of two in ten additional patients. Eight of these were still having seizures at follow-up and two had remitted; both of the latter were mentally slow. One was in regular school but a D student with a moderate behavior problem, and the other presented no behavioral difficulties but was in an ungraded class.

Intercorrelation of Findings

As had been mentioned before, the main reason for this preliminary study was the opportunity to study a large number of relationships between variables. All the information that was contained on the code sheets was punched onto IBM cards and a frequency distribution was obtained for all the variables. Variables which had appeared less than five times in the entire sample (e.g. severe head injury, hypsarhythmia, cesarean section) were eliminated and 137 variables were intercorrelated on an IBM 704 computer. A "missing data" intercorrelation program was used, which computes the product-moment correlation (Pearson r) between all pairs of variables based on only those data common to each pair of variables. The variables used are shown in the Appendix. It was hoped that this procedure would demonstrate all the variables that were significantly correlated with

"seizure state at the time of follow-up"; it would likewise show the significant correlates with behavior and/or school problems at the time of follow-up; in addition it could produce a host of relationships which are not necessarily related to prognosis but deal with more general problems in epilepsy (e.g. relationship between psychological test results and seizure frequency; family history of epilepsy and seizure type or EEG patterns). The statistically significant correlations that were obtained with the variable "seizure state at time of follow-up" are shown in Table 34.

TABLE 34

SIGNIFICANT CORRELATIONS WITH SEIZURE STATE AT TIME OF FOLLOW-UP

	r	*Significance Level* (%)
Prognosis for academic achievement	.487	1%
Amount of theta activity in EEG	.444	2%
Vocalization at onset of major seizure	.417	2%
Amount of physical illnesses	.401	5%
Duration of seizure disorder prior to evaluation	.362	5%
Seizures occurring mostly within two hours after awakening	.420	5%
Etiological factors present in history	.394	5%
Mental retardation present	.383	5%
Family history of psychiatric hospitalization	.412	5%
Seizures started during first year of life	.302	10%
Highest degree of fever attained	.498	10%
Amount of abnormality in EEG, Evaluation II	.347	10%
Amount of fast activity in EEG, Evaluation II	−.330	10%

In order to understand this and the subsequent tables, a few explanations have to be given in regard to the coding. A full description of the coding system has been published previously, Rodin *et al.* (1962). If a phenomenon was either present or absent such as specific seizure type, it was coded as 1, meaning absent, and 2, meaning present. If a phenomenon could be graded in regard to its intensity, this was done on a 9-point scale with 1 meaning "phenomenon absent" and 9, "phenomenon present to maximum extent." On occasion the normal phenomenon was placed in the middle of the scale and the two extremes on either end. Whenever a time element was involved (such as for

duration of seizure disorder or age at time of sitting up), the sequence was from the lowest to highest. Figures 1 through 3 show an example for each of the types of scales used.

At the time of coding the charts, a prognosis was given to each

CURRENT SEIZURES PRESENT SINCE

0 Not recorded
1 Less than 1 month
2 1–2 months
3 3–6 months
4 7–11 months
5 1–3 years
6 4–6 years
7 7–9 years
8 10–15 years
9 More than 15 years

FIGURE 1. Example of scale used in MEC follow-up projects

ACTIVITY DURING FIRST YEAR OF LIFE

0 Not recorded
1 Almost none
2
3 Moderately underactive
4
5 Normally active
6
7 Moderately overactive
8
9 Hyperactive

FIGURE 2. Example of scale used in MEC follow-up projects

FEEDING PROBLEMS IN INFANCY

0 Not recorded
1 None
2
3 Mild
4
5 Moderate
6
7 Marked
8
9 Severe

FIGURE 3. Example of scale used in MEC follow-up projects

patient for result of treatment in regard to seizures, behavior, and academic achievement. These prognoses were pure speculations to be confirmed or disproven at time of actual follow-up. They were based on traditional neurological criteria. Prognosis was coded from 1, meaning excellent, to 9, meaning extremely poor outcome expected. The variables listed above the broken line in Table 34 are correlated to a statistically significant degree; the correlates below the broken line show a tendency towards statistical significance. The different levels of significance with equally high or higher correlation coefficients result from unequal numbers in the separate calculations. Unless specifically stated as "Evaluation II" all variables refer to the state of the patient at time of initial examination.

Reviewing Table 34 one finds, in essence, that a good or poor outcome in regard to seizures was related to the duration of the illness, the presence or absence of possible etiological factors, mental retardation, and amount of background slowing in the electroencephalogram. These findings confirm what has been reported in the literature. There was also a suggestion that patients who had a greater number of physical illnesses did not achieve seizure control, and that patients whose seizures occurred mostly within two hours after awaking in the morning did poorly. The variable vocalization at onset of major seizure refers to the "epileptic cry" and the study suggested that this phenomenon may also carry a poor prognosis when it occurs in children.

The highest correlation coefficient was obtained—interestingly enough—with prognosis for academic achievement. This prognosis was based on the following criteria: The preschool child with normal landmarks of development, absence of mental retardation at time of examination, and absence of hyperkinetic behavior was given a good prognosis. The degree of presence of any of these criteria led to the prediction of poorer scholastic achievement. The same criteria were also applied to the school age child, but in addition, the previous school achievement was taken into account. This is, of course, a clinical way of estimating intelligence especially in the preschool child where formal testing is difficult. A point of interest in this respect is that the prognosis for seizure state received a correlation coefficient of

only .12 with the actual outcome, and this of course was not significant. I had tried to predict seizure outcome intuitively using the conventional criteria at the disposal of the clinical neurologist, and this resulted in complete failure. The data would suggest in retrospect that one might have done better in predicting seizure outcome by using the criteria for prognosis in regard to school performance. It is, however, important to point out at this time that none of the correlations shown in Table 34 as well as the subsequent tables dealing with this investigation can be taken at full face value. We must remember that we are dealing with a large number of variables and a small number of patients. This will inevitably affect the outcome of the calculations, and chance correlations are undoubtedly present. It is impossible to say which significant correlations are indeed reproducible on the basis of one sample alone. Therefore, before attaching too much weight to any given correlation, one might be better off at present to look for patterns that ring true on the basis of past experience, than to conclude firmly that a newly found correlate is indeed important.

Factor Analysis

Inasmuch as correlation coefficients give only the strength of relationship between two variables, it was of interest to see whether groups of symptoms and/or signs could be demonstrated which would show mutual relationships. It was hoped that the statistical technique of factor analysis might demonstrate syndromes that exist within a group of childhood epilepsies which might have a bearing on prognosis. The computer program available to us at that time was able to manipulate only 50 variables for factor analysis. The variables that were selected are shown in the Appendix. With principal axis solution and Varimax rotation, eight factors were obtained. Four of these were of relevance in regard to follow-up findings. Factor I deals with school achievement and will be presented later. Factor II, Table 35, points out that the EEG is likely to remain abnormal in regard to background rhythms and seizure patterns when the children were underactive during the first six months of life,

and it also suggests that the patients whose seizures start early in life continue to show EEG abnormalities. However, for the most part the factor shows that the EEG tends to behave as an independent variable. The absence of relationship to clinical sei-

TABLE 35

FACTOR II

.95	Child underactive during first year of life
.85	Abnormal EEG, Evaluation II
.84	Little alpha rhythm in EEG, Evaluation II
.81	Marked amount of theta activity in EEG, Evaluation II
.70	Seizure pattern in EEG, Evaluation II
.54	Marked theta activity in EEG, Evaluation I
.45	Early onset of convulsive disorder
.40	Seizure disorder started during first year of life
.38	Behavior problem at time of follow-up
.37	Poor alpha rhythm in EEG, Evaluation I
.33	Focal disturbance in EEG, Evaluation II
.31	Objective findings on neurological examination, Evaluation I

zure state at time of follow-up is especially notable. Factor III, Table 36, presents some of the characteristics of the patient who is likely to become institutionalized as a result of his illness. An interesting aspect of this factor is that it deals essentially with seizure intensity and it is shown here standing by itself unrelated

TABLE 36

FACTOR III

.85	Combination of seizures
.78	History of status epilepticus
.54	Long duration of individual attacks
.41	Institutionalized
.36	Minor focal motor seizures
.33	Early onset of convulsive disorder
.32	No evidence of social factors contributing to illness

to the EEG or presumed etiologies. Factor VI, Table 37, is the only one that showed some relationship to seizure state at time of follow-up. Even here the relationship is not very strong, the variable appearing quite low on the factor. Nevertheless, the factor suggests that excessively high fevers are associated with evidence

of brain damage and intellectual loss and these patients may not be controllable by medication.

To summarize some of the results of the factor analysis in regard to prognosis one could say that (1) the electroencephalogram behaves for the most part as an independent variable, but there is a suggestion that it is likely to remain abnormal in children whose seizures started in the first year of life (2) if a child has a history of repeated status epilepticus, a combination of different seizure types, and the individual attacks last a long period of time, the prognosis for making a satisfactory adjustment in the community is poor. Seizures may or may not stop after the

TABLE 37

FACTOR VI

.94	High fever
.82	Poor academic prognosis
.58	Poor behavior prognosis
.54	Low IQ
.54	Academic school problem at time of follow-up
.50	Objective findings on initial neurological examination
.49	Poor seizure prognosis
.47	Seizures same or worse
.42	Behavior problem at time of follow-up
.42	Marked theta activity in EEG, Evaluation I

patient is institutionalized, and (3) children with marked mental retardation and abnormal findings on neurological examination are likely to remain uncontrolled in regard to seizures and to present chronic behavior problems.

These conclusions have emphasized the poor outcome of patients, but the results of the factor analysis can of course also be read from the opposite point of view: (1) the EEG is likely to improve if the seizure disorder did not start in infancy; (2) a child who has only one seizure type, no history of status epilepticus, and whose major seizures are of brief duration is not likely to deteriorate to a level that will require institutionalization. The factor does not apply to patients with infantile spasms because this seizure type was not represented in the factor analysis, and (3) children who have no evidence of mental retardation

and a normal neurological examination are likely to show improvement in their seizures, and are not likely to become chronic behavior problems.

Before entering into further speculations, we have to remind ourselves that these results are merely to be taken as suggestions for future study and not as final conclusions. It has been pointed out repeatedly that we were forced to work with a small sample and this is always undesirable.

SECOND FOLLOW-UP STUDY

After we had established that the coding system could give meaningful findings, it was apparent that a larger sample of patients was needed. It was therefore decided to conduct a second follow-up study on all patients regardless of age, who fulfilled essentially the same criteria as the group of children in the first study. The age limitation was dropped in order to get as large a sample as possible. Patients qualified for inclusion in the second follow-up study by fulfilling the following criteria: (1) definite diagnosis of epilepsy as defined in the first follow-up study; (2) residence in the greater Detroit metropolitan area; (3) complete workup at the Center prior to January, 1956;— The second follow-up study was conducted between 1961 and 1962. The five-year minimum between original evaluation and follow-up was therefore maintained—, and (4) no participation in the first follow-up study.

Using these criteria, 222 patients became eligible for the study.

Eighty-six (38.7%) patients could not be reached either by mail or telephone. Of the remaining 136 patients, thirteen (9.6%) had died; thirty-three (24.3%) refused to return to the Center for reexamination. Eighty-three (61.0%) were reexamined at the Center, seven (5.1%) were found to have been institutionalized at Caro State Hospital, and these patients were transferred to the Lafayette Clinic for reevaluation. The main body of the data that will be presented subsequently deals with the results of follow-up of these ninety patients.

Before going into these results, the thirty-three patients who refused to return for reexamination should be discussed some-

what further. It might be assumed that these patients had, in the majority, enjoyed a long remission and by concentrating on patients who in fact returned for reexamination one would *a priori* deal with a negative selection. All of these thirty-three patients had been contacted by telephone and reasons for not wanting to be reexamined were given as follows:

1. Seizures had stopped—nine (27.3%)
2. Are working and do not want to take time off from work—eight (24.2%)
3. Various excuses, for instance, has a bad heart; does not want to come in; cannot get transportation; does not want any more examinations—seven (21.2%)
4. Are being treated elsewhere and see no point in further examinations—five (15.2%)
5. Agreed to return for reevaluation, but failed to keep appointments—four (12.1%)

In the group of nine patients who had stated that they had achieved complete seizure control, the length of remission was given as ten years in two, seven years in three, and five years in one. Three patients merely stated they "don't have spells anymore."

On basis of this admittedly meager information we could say that six patients had shown a terminal remission of at least five years' duration. This would amount to 18.1 per cent of the group who were not formally reexamined. This number is presented here only in order to allow some comparison later on with the group that was, in fact, reexamined.

As far as the thirteen patients who had died were concerned, three (23.1%) had been institutionalized and had died at Caro State Hospital. Table 38 lists the causes of death as given on the death certificates, the age at time of death, and the age at time of onset of the seizure disorder for all thirteen patients.

If we exclude the three patients with brain tumors, we find the mean age at time of death to have been 18.5 years. The mean duration of the seizure disorder was nine years. As far as the three patients with brain tumor are concerned the diagnosis had clearly been missed in the seventy-year-old patient. In the other two cases, epilepsy had preceded the detection of the tumor by

fifteen and nine years. Both of these patients had started with seizures during adolescence, which is a rather common age of onset for epilepsy of unknown cause. This reemphasizes the need for continued medical supervision, even of relatively long-standing cases of seizure disorders.

As far as the institutionalized group is concerned, it has been mentioned that it amounted to only 5 per cent of this sample. This is smaller than the 18 per cent observed in the first follow-up study. The finding is explainable by the fact that the second

TABLE 38

CAUSE OF DEATH

		Age at Time of	
		Death	*Onset*
M.D.	Brain tumor—died 8 days postoperatively	70	69
D.L.	Brain tumor—did not survive operation	32	17
E.W.	Brain tumor—did not survive operation	22	13
I.F.	Acute pulmonary embolism	60	39
T.B.	Diabetes—hypoglycemic shock	10	4
M.V.	Epilepsy (aspiration pneumonia)	19	13
R.J.	Epilepsy (aspiration of gastric contents)	10	7 months
P.S.	Epilepsy (adrenal insufficiency)	9	2
M.P.	Epilepsy (autopsy refused by parents)	1	5 weeks
C.H.	Status epilepticus	20	17
A.M.	Drowning	35	10
J.R.	Drowning	17	12
R.K.	Drowning	14	7

study dealt predominantly with older patients. If we limit ourselves to the twenty-seven patients who were ten years old or younger when first seen at the Center, we find that six (22.2%) of them had become institutionalized. This percentage is quite similar to that obtained from the sample in the first follow-up study.

Turning our attention now to the ninety patients who were reexamined either at the Center or the Lafayette Clinic, it should be mentioned that prior to reexamination of each patient the initial history was coded in the same manner as for the first follow-up study and a prognosis was assigned to each patient on

basis of this information. The patient was then seen in neurological evaluation; an interval history was obtained, and specific historical information about birth and early development, which had on occasion been lacking in the patient's chart, was supplemented. The mental status of the patient was evaluated and coded, all patients had another electroencephalogram; but most of them did not go to sleep during the tracings. The patients who were on anticonvulsant medication were not taken off their drugs prior to the EEG. Eighty-five (94.4%) patients were given a Bender-Gestalt test; the WAIS was administered to fifty-four (60.0%) patients, and the WISC was given in fourteen (15.5%) instances. All this material was recorded on the coding forms and transferred onto IBM cards.

Description of Sample

The duration of follow-up is shown in Table 39. There were forty-nine males and forty-one females in the group. Table 40

TABLE 39

DURATION OF FOLLOW-UP

Years	12	11	10	9	8	7	6	5
Patients	2	5	7	14	9	14	20	19

contains the seizure types that had been present at time of initial evaluation. Forty-two (46.6%) patients had one seizure type only; two (2.2%) had major seizures and intermittently only auras; thirty-nine (43.3%) had two distinct seizure types; six (6.7%) had three seizure types, and one had four different types

TABLE 40

SEIZURE TYPES

Nonfocal grand mal	41
Focal grand mal	30
Psychomotor seizures	21
Absence	20
Focal minor motor seizures	12
Myoclonic jerks, myoclonic seizures or akinetic seizures	12
Nonfocal minor motor seizures	5
Psychic or sensory seizures	3

of attacks. The term "absence" refers to the clinical description of the attack and is not necessarily synonymous with 3 cycles per second spike wave activity in the EEG, or "pure petit mal."

As far as etiology was concerned, none could be ascertained in fifty-one cases (56.6%); various degrees of birth injuries were reported in twenty-nine (32.2%); postnatal head injuries that could have been of etiological importance were noted in eight (8.8%); cerebral infections in eleven (12.2%); a positive family history of epilepsy was present in thirty-five (38.8%), and thirteen (14.4%) patients had evidence for a family history of epilepsy as well as some added insult to the central nervous system. These figures do not add up to ninety because some patients had evidence of more than one type of insult to the central nervous system. All the patients except four had been on anticonvulsant medication prior to their first visit to the Center. The anticonvulsant regime was judged adequate in terms of type of drug and dosage for the particular seizure type in sixty-one (67.7%), and inadequate in twenty-five (27.7%) patients. Nine (10.0%) patients had suffered from grand mal status epilepticus. In order to avoid duplication, the description of the sample in terms of age when first seen, age at time of onset of seizures, intelligence, et cetera, will be shown in relation to follow-up results and will therefore be omitted here.

Results

Twenty-nine patients (32.2%) had become seizure free for two years or more prior to reevaluation; twenty-seven (30.0%) had shown some improvement in regard to frequency of occurrence or severity of seizures, and thirty-four (37.7%) had remained essentially unchanged or become somewhat worse. Seizure freedom for five years or more had been achieved in fifteen patients of the total group (16.7%), and one patient had been seizure free for ten years (7.1% of fourteen patients who had been followed for ten years or more). It is interesting to note here that a two-year terminal remission had occurred in the same proportion of cases in this study as in the first one (32.2% versus 33.0%). The five-year remission rate was lower in this second

group than in the first (16.7% versus 29.0%). Ten patients had stopped taking anticonvulsant medication; eight of these had been seizure free for three to seven years; two were still having seizures but drug treatment was discontinued by the parents. One of these patients was profoundly retarded mentally, had myoclonic jerks and myoclonic seizures for which drug treatment had been totally ineffective. The patient's mother had therefore stopped buying medications. The other patient had clear-cut evidence of petit mal during the follow-up electroencephalogram, but the mother had felt that the patient's seizures had improved to an extent that treatment was no longer needed.

TABLE 41

MAJOR SEIZURES

	Frequency of Maximal Occurrence	*Frequency at Evaluation I*	*Frequency at Evaluation II*
Less than once a year	0	7	30
About once a year	4	6	3
2 to 3 seizures per year	5	7	6
4 to 6 seizures per year	1	6	7
7 to 12 seizures per year	3	6	8
About once a month	6	11	2
2 to 3 a month	9	6	10
Once a week	3	3	2
More than once a week	40	19	3

As far as major seizures were concerned, forty patients (44.4%) had at one time experienced more than one seizure per week and only nine (10.0%) had had less than three seizures per year. Table 41 shows the tendency for improvement of major seizures. We can see that by the time the patients were initially seen at the Center, seizures for the most part had already decreased in frequency from their maximum and they had further decreased by the time of second evaluation. The same phenomenon can be observed for minor seizures, shown in Table 42.

As far as the EEG is concerned the initial tracings could be evaluated in seventy-eight cases. In twelve instances the record was either technically poor or the tracings had been obtained at a local hospital and only the EEG report was available in the

TABLE 42

MINOR SEIZURES

	Frequency of Maximal Occurrence	*Frequency at Evaluation I*	*Frequency at Evaluation II*
Less than once a year	0	0	24
About once a year	0	0	1
2 to 3 seizures per year	1	2	2
4 to 6 seizures per year	2	5	2
7 to 12 seizures per year	2	4	1
About once a month	2	1	0
2 to 3 a month	1	1	6
Once a week	1	4	1
More than once a week	39	31	11

chart. These seventy-eight tracings were then compared with the ones obtained at follow-up. The results in regard to overall EEG abnormality, seizure patterns, and focal abnormalities are shown in Tables 43, 44, and 45.

TABLE 43

AMOUNT OF EEG ABNORMALITY

	Initial EEG	*Follow-up EEG*
Normal	18	11
Borderline	12	7
Mildly abnormal	10	15
Moderately abnormal	24	23
Markedly abnormal	14	22

The EEG had stayed the same in twenty-seven patients, deteriorated in twenty-four, and improved in twenty-two. It had been normal on both evaluations in five patients.

TABLE 44

SEIZURE PATTERNS

	Initial EEG	*Follow-up EEG*
No seizure patterns	30	34
Questionable	9	7
Mild	14	13
Moderate	18	17
Marked	7	7

TABLE 45
FOCAL ABNORMALITIES

	Initial EEG	*Follow-up EEG*
None	54	44
Mild	8	15
Moderate	10	11
Marked	4	6

Twenty-two patients had had no seizure patterns in their tracings at either evaluation; twenty had remained the same in regard to the amount of seizure activity; eighteen had improved, and eighteen had deteriorated.

Thirty-three patients had had no focal findings in either recording; twenty-three had deteriorated; eleven improved, and nine had stayed the same in this respect. In two instances no comparison was possible because information was missing on the first trace.

Reviewing these tables we find that in contrast to the clinical picture the EEG had in general not shown appreciable improvement; it had actually deteriorated somewhat. This deterioration was not due to an increase in seizure patterns but to an increase in focal abnormalities. These findings are therefore in contrast to the observations of the first follow-up study. The question arises again whether the age difference between these two groups was the decisive factor for the different results. The information summarized in Tables 46, 47, and 48 was applicable to a study limited to twenty-five children who were age ten or younger at initial evaluation and who had two satisfactory EEGs.

TABLE 46
AMOUNT OF EEG ABNORMALITY
AGE 10 OR YOUNGER

	Initial EEG	*Follow-up EEG*
Normal	7	4
Borderline	4	4
Mildly abnormal	1	2
Moderately abnormal	3	7
Markedly abnormal	10	8

The EEG had improved in regard to overall amount of abnormality in six patients; it had deteriorated in seven; it had remained the same in nine; it had been normal on both occasions in three. EEG seizure patterns had improved in four patients, deteriorated in five, had remained the same in seven, and nine

TABLE 47
SEIZURE PATTERNS
AGE 10 OR YOUNGER

	Initial EEG	*Follow-up EEG*
No seizure patterns	12	12
Questionable	1	3
Mild	1	2
Moderate	6	4
Marked	5	4

patients had not had seizure patterns on either occasion. Focal disturbances had improved in four, deteriorated in four, and sixteen patients had not had focal abnormalities on either occasion. Focal abnormalities could not be adequately evaluated in the first tracing of one patient and the comparison was therefore based on 24 individuals.

TABLE 48
FOCAL ABNORMALITIES
AGE 10 OR YOUNGER

	Initial EEG	*Follow-up EEG*
None	20	20
Mild	3	2
Moderate	0	2
Marked	1	0

The tendency towards improvement of the EEG was therefore not borne out in this particular sample and this reemphasizes the caution one has to use when one compares percentage figures based on small samples. It also points out the necessity of using tests for statistical significance of the data.

Intercorrelation of Findings

As mentioned before, the main goal of this investigation had been to find prognostic criteria especially in regard to seizure control. To accomplish this, frequency distributions were obtained for the entire material, and 155 variables were then selected for intercorrelation. They are shown in the Appendix. The rule was adopted that each variable had to have been present in at least ten individuals; but this rule unfortunately prevented the inclusion of the variable "state hospitalized at time of follow-up" because only seven individuals had fallen into this category. An exception was made for grand mal status epilepticus. Although it had occurred in only nine individuals, its omission from computations would have been regrettable.

Correlations with Seizure Outcome

Table 49 lists the statistically significant correlations with the variable seizure state at time of follow-up with data obtained at the time of the initial evaluation.

TABLE 49

SIGNIFICANT CORRELATIONS BETWEEN FINDINGS FROM INITIAL EVALUATION AND SEIZURE-STATE AT TIME OF FOLLOW-UP

	r	*Significance Level* (%)
Psychomotor seizures	.323	1
Combination of different seizure types	.294	1
Prognosis for seizure control	.277	1
Duration of seizure disorder	.276	2
Seizure patterns in EEG	.265	5
Grand mal status epilepticus	.263	5
Psychiatric diagnosis in addition to diagnosis of epilepsy	.255	5
Spike wave activity in EEG	.230	10
Amount of abnormality in EEG	.200	10
Female sex	.198	10
Prognosis for behavior	.188	10

Reviewing Table 49 we find that a poor outcome in regard to seizure control seemed to depend mostly upon (1) psychomotor seizures, (2) presence of more than one seizure type, (3) long duration of the illness, (4) history of grand mal status epilepticus, and (5) marked seizure patterns in the initial EEG. Female patients showed a tendency towards poorer outcome, but this did not reach statistical significance. It is of interest that prognosis for seizure control was significantly correlated (although the correlation coefficient was still quite low) with seizure outcome in this particular sample. This suggests that prognostication may be easier in a predominantly adolescent and adult population than in children.

Table 50 lists the variables that had shown significant correlates with seizure state; but were obtained at the time of re-evaluation.

One can note that patients whose seizures persisted tended to have either psychiatric difficulties and/or organic mental

TABLE 50

SIGNIFICANT CORRELATES BETWEEN FINDINGS OBTAINED AT FOLLOW-UP EXAMINATION AND SEIZURE-STATE AT FOLLOW-UP

	r	*Significance Level* (%)
Behavior problem	.417	1
Seizure patterns in EEG	.393	1
Proverb interpretation concrete	.391	1
Amount of abnormality in EEG	.372	1
Response to adequate amounts of anticonvulsant medication	−.305	2
Combination of different seizure types	.308	5
Psychomotor seizures	.280	2
Focal sharp waves in EEG	.277	2
Amount of theta activity in EEG	.272	2
History of depression	.263	5
Organic mental changes	.240	5
Personality disorder	.244	5
Amount of focal disturbance in EEG	.228	5
Amount of alpha activity in EEG	−.211	10
Academic school problem	.352	10
Spike wave activity in EEG	.209	10

changes. The EEG tended to be abnormal, showing diffuse or focal seizure patterns and/or marked theta activity. If we now compare Table 34 from the first follow-up study with Tables 49 and 50 from the second study, we find that we have not made any discovery that has not been mentioned some place in the literature. Practically each one of these findings has been reported in the past to be associated with a poor outcome if present, and a good outcome if absent. What is more interesting, and also discouraging, is the fact that there is hardly any overlap between the results of the two studies. What was statistically significant in one failed to show statistical significance in the other. Although we could blame the age difference again, it is important to point out that repetition of findings in regard to seizure outcome is not easy, and this is probably the major reason for the divergent opinions in the literature. The only finding that showed significant correlation with seizure state at time of follow-up in both studies was duration of seizure disorder prior to initial evaluation. We will return to this particular aspect later in more detail.

FACTOR ANALYSIS

As mentioned at the time of discussion of the first follow-up results, one is not only interested in relationships between a pair of variables, but one would like to know which of these symptoms and signs form a group that would relate to prognosis. Therefore, a factor analysis was again performed. The ninety variables that were included in the factor analysis are shown in the Appendix. Principal axis solution and Varimax rotation were used and fourteen factors were extracted. The first factor is shown in Table 51. It demonstrates the characteristics of the chronic epileptic patient with brain damage. The seizures express themselves clinically most consistently in the form of focal minor motor attacks. If we view the factor from the opposite side we find that patients with normal IQ, normal Bender-Gestalt test performance, normal landmarks of development, and normal neurological examination tend to have a good prognosis for seizures and employment. This expresses in factorial form the opinions that have been stated

TABLE 51

FACTOR I

.96	Low Full Scale IQ, Evaluation II
.96	Low Full Scale IQ, Evaluation I
.91	Low Verbal IQ, Evaluation II
.91	Low Verbal IQ, Evaluation I
.86	Low Performance IQ, Evaluation I
.85	Low Performance IQ, Evaluation II
.78	Bender test rated "organic", Evaluation I
.77	Present seizure-state same or worse, Evaluation II
.68	Organic mental syndrome, Evaluation II
.48	Late onset of talking age
.46	Received special schooling
.44	Immaturity on psychological testing, Evaluation I
.43	Objective neurological findings, Evaluation I
.38	Symptom present during first year of life
.36	Focal minor motor seizures, Evaluation I
.34	Not employed, Evaluation II

in the literature. The factor as presented in Table 51 could be called "epilepsy associated with cerebral damage." The damage tends to occur most frequently in infancy and early childhood, but it should be pointed out that the factor loadings for the variables dealing with age relationships begin at .48 and are not high on the list. This suggests that onset in childhood, although common, is not a necessary prerequisite.

The second factor, Table 52, deals almost exclusively with

TABLE 52

FACTOR II

.89	Seizure patterns in EEG, Evaluation I
.85	EEG abnormal, Evaluation I
.72	Seizure patterns in EEG, Evaluation II
.70	EEG abnormal, Evaluation II
.57	Marked amount of theta activity, Evaluation II
.57	Generalized paroxysmal activity, Evaluation II
.53	Generalized paroxysmal activity, Evaluation I
.52	Spike wave activity, Evaluation I
.48	Spike wave activity, Evaluation II
.39	Absence—myoclonic jerks, myoclonic seizures and/or akinetic seizures, Evaluation I
.33	Poor alpha rhythm, Evaluation II
.31	Present seizure-state same or worse, Evaluation II

EEG characteristics. It suggests that a tracing which contains seizure patterns when the patient is already on some anticonvulsant medication is not likely to become completely normal later. Seizure patterns tend to persist and the EEG background tends to slow down to the theta frequency range. Clinically, one finds most commonly a member of Lennox's petit mal triad. It has been mentioned in the literature review that these various clinical conditions do not necessarily represent a homogeneous sample, but they were placed into one group for the intercorrelations and factor analysis in order to increase the number of patients with which one is dealing. Pure petit mal absences had occurred in six patients only, and it would not have been possible to perform adequate statistical studies. Classical three cycle per second spike wave activity was not included for the same reason. The factor expresses the observation reported in the literature that seizure activity in the EEG is related to the overt clinical seizure state only to a relatively minor degree. The factor might be called "EEG seizure activity." The next seven factors did not deal with prognostic information and will not be presented here.

Factor IX, Table 53, represents what might be called "mixed psychomotor epilepsy." It shows the characteristics of a segment of the epileptic population that tends to be resistant to our current anticonvulsant drug regime. It is the only factor where seizure outcome heads the list of variables. It also shows that the organic mental syndrome is usually not too pronounced in this

TABLE 53

FACTOR IX

.70	Present seizure-state same or worse
.61	Behavior problem at follow-up
.50	Psychomotor seizures, Evaluation I
.49	Personality problem, Evaluation II
.39	Proverb interpretation concrete, Evaluation II
.38	Verbal less than Performance IQ, Evaluation I
.37	Psychiatric diagnosis made in addition to diagnosis of epilepsy, Evaluation I
.34	Social factors contributing to illness
.33	Combination of seizures, Evaluation II
.30	Little personal relationships during adolescence
.30	Not employed, Evaluation II

group of patients because it appears on the factor only as concrete proverb interpretations. Furthermore, the factor points out that psychomotor epilepsy and behavioral difficulties are indeed fairly commonly related.

Factor X is shown in Table 54 because it points to the existence of what might be called the "specific seizure propensity" of the individual. It is somewhat akin to Factor III of the first study. It shows essentially that frequency of recurrence of seizures is unrelated to presumed etiology as well as neurologic, psychiatric, psychologic, and electroencephalographic observations. This factor can therefore be regarded as the nucleus of the epilepsy problem. Until we find variables that relate to this factor we are likely to remain in the dark about the real cause of the disorder. The term "seizure propensity" rather than "seizure threshold"

TABLE 54

FACTOR X

.77	Frequent grand mal seizures at time of Evaluation I
.69	History of frequent grand mal seizures prior to Evaluation I
.52	History of clusters of seizures per day, Evaluation I
.38	No, or, brief remission of major seizures prior to Evaluation I

was chosen because the latter has acquired a very specific meaning in regard to the ease with which seizures can be induced in normals or epileptics by means of drugs or electricity. As will be shown later, the "seizure threshold" of the individual (i.e. amount of drug needed to induce an epileptic attack) is *not* related to his "seizure propensity" (i.e. the tendency of the individual towards *recurrent* seizures). This latter tendency is a totally separate phenomenon and constitutes the core of the epilepsy problem.

To summarize the results of this factor analysis we could say (1) patients who show an organic mental syndrome and low IQ are likely to have an uncontrolled seizure disorder and an illness that dates to early childhood; (2) the EEG behaves for the most part as an independent factor of its own, but diffuse paroxysmal activity is frequently linked to one of the forms of Lennox's petit mal triad; (3) a considerable number of chronic epileptic pa-

tients are likely to show evidence of temporal lobe seizures, personality difficulties, and organic mental changes, and (4) there exists a factor of specific "seizure propensity" which is essentially unrelated to the information that is currently obtained in the workup of our patients. This factor represents the core of the epilepsy problem.

Analysis of Variance

Data analysis up to this point had led to interesting observations but it had not provided firm criteria upon which prognosis for seizure control could be based. A source of disappointment was the fact that only one correlate had appeared in both follow-up studies as significantly related to seizure outcome. This was the variable "duration of illness." The two studies had been in much better agreement in regard to criteria for behavior and school achievement, as will be shown later; but unless we can find significant relationships to seizure control, with findings that can be obtained at the first examination of the patient, we cannot realistically say that we have accomplished very much in regard to prognosticating the course of epilepsy.

The results presented so far have been based on a correlational analysis. Of equal interest are any mean differences in the variables between our various groups of patients. To study these differences, an analysis of variance was used.

The ninety patients were divided into three groups: (1) completely controlled for at least two years, twenty-nine patients; (2) improved but still having seizures, twenty-seven patients, and (3) essentially no change since initial evaluation or deterioration, thirty-four patients. Variables that showed a continuous distribution such as age, number of seizure types, amount of EEG abnormality were subjected to the F test. For variables that had been coded as dichotomies such as sex, seizure type, seizures present during first year of life, the Chi Square test was used. Altogether 190 variables were then selected from the initial evaluation and examined in this manner. The list of variables used is included in the Appendix. Inasmuch as we are concerned about prognosis, data obtained on follow-up examination were not in-

eluded except for summary statements dealing with behavior, school achievement, employment, and overall condition of the patient. Table 55 shows the statistically significant results of the F tests, and Table 56, the statistically significant results of the Chi Square tests. Variables that had previously shown statistically significant correlation coefficients are marked by an asterisk. It was gratifying to see that all the variables that had shown significant relationships in the correlation matrix were represented in Tables 55 and 56, in spite of the different statistical methods. We are therefore dealing with correct observations that had occurred in this sample of patients and not with statistical artifact. The variables that do not carry an asterisk in Tables 55 and 56 had either not been included in the initial correlation matrix (the intercorrelation program had only allowed processing of 155 variables) or had shown a tendency towards statistical significance—for instance, amount of EEG abnormality. If we concentrate now on the findings obtained in the controlled group, we see the following important features:

1. The controlled group was the youngest.
2. More than one different seizure type was least common.
3. The seizure disorder was of shorter duration.
4. Injuries as a result of major seizures were infrequent.
5. The EEG recordings showed less seizure activity when the patients were first seen.
6. The EEG tracings showed also a lesser amount of overall abnormalities.
7. A tendency towards clusters of seizures over a few days with subsequent freedom from seizures for a few weeks was uncommon.
8. Psychomotor seizures were uncommon.
9. Psychiatric difficulties were not of major degree (i.e. no treatment recommended in most instances).
10. The patients' immediate response to anticonvulsant medication tended to be better.

The last point is in agreement with the observation by Lund (1966) that treatment results during the first three months cor-

TABLE 55

SIGNIFICANT DIFFERENCES BETWEEN PATIENTS RELATED TO FOLLOW-UP STATE

	Controlled	*Improved*	*Unchanged or Worse*	*F*	*Significance Level (%)*
Frequency of injuries during major seizures	2.8	3.3	5.2	9.0	1
Combination of seizures*	1.4	2.6	2.5	7.7	1
Behavior problem at follow-up*	1.9	2.6	3.6	7.4	1
Age	13.6 years	24.1 years	19.3 years	6.8	1
Amount of seizure patterns in initial EEG*	2.8	3.8	5.2	5.1	1
Duration of seizure disorder* (major seizures)	5.6	7.2	7.1	4.9	1
Amount of EEG abnormalities	4.6	6.2	6.7	3.6	5
Duration of seizure disorder* (minor seizures)	5.5	7.1	6.8	3.3	5
Picture Arrangement (Wechsler IQ)	9.6	7.7	10.1	3.3	5
Prognosis for seizure control*	3.9	4.6	5.0	3.2	5
Object Assembly (Wechsler IQ)	9.7	8.4	11.0	3.2	5
Frequency of tongue biting during major seizures	3.2	4.4	5.3	2.9	10
Block Design (Wechsler IQ)	8.3	8.0	10.2	2.8	10
School truancy	2.8	1.4	2.3	2.7	10
Immaturity on psychological tests	5.6	6.8	6.2	2.6	10
Initial response to anticonvulsant medication	4.1	3.6	2.0	2.5	10
Performance IQ	94.1	87.9	99.3	2.5	10

TABLE 56

SIGNIFICANT DIFFERENCES BETWEEN PATIENTS RELATED TO FOLLOW-UP STATE

		Controlled	*Improved*	*Unchanged or Worse*	X^2	*Significance Level (%)*
Clusters of major seizures for several days, freedom from seizures for several weeks						
	Absent	22	14	20	9.3	1
	Present	0	8	7		
Amount of diffuse delta activity in EEG						
	Absent	15	21	25	8.1	2
	Present	8	4	1		
History of severe infectious disease						
	Absent	18	25	24	7.2	5
	Present	11	2	10		
Psychiatric treatment recommended						
	Absent	28	24	25	7.0	5
	Present	1	3	9		
Psychomotor seizures*						
	Absent	27	18	24	6.5	5
	Present	2	9	10		
Cyanotic during major seizures						
	Absent	18	16	14	5.9	10
	Present	4	7	14		
Family history of meningitis						
	Absent	28	20	28	5.3	10
	Present	1	6	3		
Psychiatric diagnosis made in addition to diagnosis of epilepsy*						
	Absent	28	25	27	5.1	10
	Present	1	2	7		

related well with the course of the illness in the following year.

As far as grand mal status was concerned, the difference between the groups was not significant statistically, but the distribution was in the expected direction as shown in Table 57. In eighteen patients there was no definite information in the charts in this particular respect.

The interesting feature emerging from the analysis of variance is that presumed etiologies like birth injury, postnatal head injury, infection, or heredity were not relevant for seizure prognosis. Objective findings on neurological examination, poor school performance, and organic findings on psychological tests also did not preclude a terminal remission of at least two years.

The fact that age at time of initial evaluation was a significant variable in regard to seizure control is important because it

TABLE 57

	Controlled	*Improved*	*Same or worse*
Grand mal status			
Absent	21	21	21
Present	1	1	7

places the entire problem of prognosis into a different light. We can see that the group which had enjoyed a terminal remission of at least two years was the youngest with a mean age of 13.6 years, but the same or worse group—which one would regard as the worst off—stood in the middle, and the improved group contained the older patients. This was a somewhat unusual distribution, especially when we compare it with other findings such as frequency of injuries during major seizures, amount of seizure patterns, amount of EEG abnormality, or prognosis for seizure control where the improved group did indeed occupy an intermediate position. It was therefore important to look at the actual distribution of the follow-up results in regard to the age at which the patients were first seen at the Center.

Table 58 shows the relationships between seizure outcome and age at the time of initial visit arranged by decades. We can immediately see an interesting phenomenon. Children up to ten

TABLE 58

AGE AT TIME OF INITIAL EVALUATION AND SEIZURE-STATE AT FOLLOW-UP

Years	*0–10*	*11–20*	*21–30*	*31–40*	*41–52*	*Total*
In remission for at least 2 years	13	10	4	2	0	29
Improved	4	8	7	5	3	27
Unchanged or Worse	11	6	10	7	0	34
Total	28	24	21	14	3	90

years of age showed either a complete remission or remained essentially unchanged. Only four took the intermediate position of improvement. Patients seen in the second decade of life were, for the most part, either completely controlled or improved; but from the third decade on, complete control became markedly less common and the patients tended to fall either into the improved or unchanged/worse group.

Significant Differences among Groups Depending upon Age at which Patient is First Seen at a Specialized Center

The fact that age is an important variable for seizure prognosis having been established, it was of interest to see what the main differences are in a population of epileptic patients when they are divided on the basis of age at time of their first visit to a specialized center. The group of ninety patients was subdivided into twenty-eight patients ranging in ages between one and ten years, thirty-six patients in ages eleven to twenty-five years, and twenty-six patients from twenty-six to forty-four years. These three groups were compared on the same 190 variables that had been used in regard to seizure state at time of follow-up. The main results for the F tests and the Chi Square tests are shown in Tables 59 and 60.

The important features in regard to prognosis can be summarized as follows:

1. Adolescents and young adults tended to do best in regard to response to anticonvulsant medication, seizure state at follow-up (which does not necessarily imply com-

plete control), intellectual functions, neurological examination, and they had the least "organic" dysfunctions on psychological testing.

TABLE 59

SIGNIFICANT DIFFERENCES BETWEEN PATIENTS DEPENDING UPON AGE AT INITIAL EVALUATION

	1–10 Years	*11–25 Years*	*26 years or older*	*F*	*Significance Level (%)*
Duration of seizure disorder (Major seizures)	5.3	6.0	8.6	28.8	1
Duration of seizure disorder (Minor seizures)	5.2	6.4	8.3	18.9	1
Organic pathology (Bender-Gestalt test)	5.8	2.4	4.3	11.1	1
Organic pathology suspected on other psychological tests	5.2	2.4	4.2	9.9	1
Frequency of injuries during major seizures	2.5	3.8	4.9	6.0	1
Object Assembly—Wechsler IQ	7.1	10.7	9.8	5.3	1
Psychotic tendencies on psychological tests	3.2	1.6	3.0	5.2	1
Overall condition of patient	3.8	3.2	4.6	4.5	5
Prognosis for seizure control	4.5	4.0	5.3	4.3	5
Clusters of grand mal seizures over several days, freedom from seizures for several weeks	1.1	1.5	2.3	4.0	5
Prognosis for behavior	4.6	3.7	5.0	3.9	5
Personality disturbances (Psychological tests)	5.6	6.2	7.4	3.9	5
Prognosis for intellectual functions	5.4	3.8	4.6	3.7	5
Grand mal status epilepticus	2.0	1.2	1.0	3.5	5
Comprehension—Wechsler IQ	7.3	10.1	8.8	3.5	5
Amount of fast activity—EEG	3.6	2.4	3.7	3.4	5
Objective findings on neurological examination	2.8	1.5	2.1	3.4	5
Amount of theta activity—EEG	5.0	4.9	3.7	3.3	5
Talking age	5.1	3.8	3.9	3.2	5
Seizure-state at follow-up	2.9	2.6	3.8	3.1	5
Response to anticonvulsant medication within first year of treatment	3.4	5.0	2.7	3.1	5

TABLE 60

SIGNIFICANT DIFFERENCES BETWEEN PATIENTS DEPENDING UPON AGE AT INITIAL EVALUATION

	1–10 Years	*11–25 Years*	*26 years or older*	X^2	*Significance Level* (%)
Family history of breathholding spells					
Absent	16	34	24	19.0	1
Present	10	2	0		
Seizure disorder started during first year of life					
Absent	10	29	22	13.6	1
Present	8	2	2		
Rotation of Bender-Gestalt figures					
Absent	4	29	15	13.3	1
Present	9	5	10		
Family history of chronic headache					
Absent	9	23	19	10.8	1
Present	17	13	5		
Seizures present during first year of life regardless of type and whether isolated or recurrent					
Absent	18	34	22	9.9	1
Present	10	2	4		
Anticonvulsant treatment discontinued by the *time of follow-up*					
No	19	33	26	9.9	1
Yes	7	3	0		

Diagnosis of psychiatric disorder made in addition to epilepsy						
	No	26	35	19		
	Yes	2	1	7	9.5	1
Emotional stress precipitating major seizures						
	No	17	24	13	8.9	5
	Yes	1	7	11		
Focal minor motor seizures						
	Absent	20	33	25	8.4	5
	Present	8	3	1		
EEG—left temporal focus						
	Absent	24	31	16	8.3	5
	Present	0	2	5		
Behavioral difficulties in school						
	Absent	20	32	25	7.2	5
	Present	8	4	1		
History of febrile convulsions						
	Absent	17	30	23	7.0	5
	Present	11	6	3		
Confusion after major seizures						
	Absent	18	22	17	6.7	5
	Present	0	9	7		
Fatigue after major seizures						
	Absent	15	18	11	6.1	5
	Present	3	13	13		

2. The group of children had the most recent onset of seizure disorders but also showed the most marked organic pathology, and grand mal status was most common in this age group.

3. The adult group had the longest duration of the seizure disorder. The patients likewise showed organic changes, and although doing better at follow-up in regard to seizure state than the children, they were the worst off in their overall functions mostly because of intellectual deficits and/or behavioral problems.

The finding that a left temporal EEG focus was age related, but not a right temporal focus, is of theoretical interest but would require validation on another sample. The significant differences in regard to the variables dealing with family history may merely reflect the possibility of obtaining more detailed historical information in the younger age group. The same applies to the personal history of febrile convulsions.

Significant Differences among Groups Depending upon Age at Time of Onset of Recurrent Seizures

The data having shown that chronological age at which the patient presents himself to a specialized center is of importance for his overall prognosis, and having shown also that duration of the seizure disorder prior to his first visit is another important consideration, it became imperative to investigate in detail the question of whether age at time of onset of the illness is important for the patient's seizure prognosis. This particular variable was originally not included in the coding forms, but it was available in the charts of the patients. The material could be divided into three approximately equal groups: onset within first three years of life, twenty-seven patients; between four and twelve years, thirty-one patients; and between thirteen to twenty-seven years, thirty patients.

Age of onset is, however, not as clear a variable as chronological age. The main problem is that a number of patients have one or two isolated febrile or afebrile seizures in infancy and have subsequently no difficulties until school age, puberty, or late

adolescence, at which time the chronic seizure disorder starts to develop. An arbitrary decision was made to regard as age of onset the time at which repeated attacks appeared, not the first isolated episode. The three groups were then compared on the previously mentioned 190 variables, and the statistically significant findings in regard to seizures are shown in Table 61. Significant findings in regard to intelligence will be presented later.

TABLE 61

SIGNIFICANT DIFFERENCES BETWEEN GROUPS DEPENDING UPON AGE AT TIME OF ONSET OF RECURRENT SEIZURES

	0–3 Years	*4–12 Years*	*13–27 Years*	*F*	*Significance Level (%)*
Amount of EEG abnormality	5.0	7.0	5.3	4.0	5
Seizure prognosis	5.3	4.0	4.3	3.8	5

		0–3 Years	*4–12 Years*	*13–27 Years*	X^2	*Significance Level (%)*
Emotional stress precipitating major seizure						
	Absent	19	20	15	11.3	1
	Present	3	2	13		
Family history of breathholding spells						
	Absent	17	26	29	9.2	1
	Present	7	5	0		
Postictal confusion after major seizures						
	Absent	20	19	17	7.3	5
	Present	4	3	11		
Family history of breech birth						
	Absent	22	25	29	6.5	5
	Present	2	6	0		
Absence						
	Absent	25	20	23	6.4	5
	Present	2	11	7		
Focal minor motor seizures						
	Absent	20	27	29	6.1	5
	Present	7	4	1		

It was interesting to see that although the youngest group was given the poorest prognosis for seizure control, the actual outcome did not differ between the three groups. As far as seizure patterns were concerned, the sample agreed with the literature that absences tend to start mostly between the ages of four and twelve, and during adolescence. A predominant seizure pattern of infancy and early childhood appears to be focal minor motor attacks. There was no significant difference in regard to focal or nonfocal major seizures, and in regard to psychomotor automatisms. The latter finding seems to be somewhat surprising because it is well known that psychomotor automatisms do not start in infancy. The explanation lies in the fact that they appeared, for the most part, as a second seizure type later in life and were then equally represented in all three groups.

The two variables dealing with family history of breech birth and breathholding spells are of potential interest but will have to be verified on another sample before one can attach clinical significance to the findings. The incidence of family history of epilepsy was not significantly different between the groups.

The EEG showed a somewhat unexpected behavior in this sample. The most marked amount of abnormality occurred in the group of patients that started with epilepsy between four and twelve years of age. The important feature of this aspect of the study was the negative observation that age of onset by itself was not significantly related to seizure outcome.

Duration of Illness

We still have to discuss the observation that duration of illness prior to first visit to the Center was the only finding that had been significantly related to seizure outcome in the first as well as the second follow-up study. A detailed breakdown of duration of illness in relation to terminal remissions revealed a somewhat surprising phenomenon as shown in Table 62.

Six of the seven patients who were seen within the first year of their illness had enjoyed complete remissions; but with those patients seen during the second year, the remission rate had

TABLE 62

RELATIONSHIP OF DURATION OF ILLNESS TO SEIZURE CONTROL

Initial Evaluation after Onset of Illness	*Number of Patients in Group*	*Number of Patients in Remission for at least two years*	*Percentages*
Within first year	7	6	85
Within second year	12	6	50
Within third year	9	3	33
Within fourth year	7	2	28
From 5 to 10 years	19	7	36
More than 10 years	36	5	13

dropped to one-half. With those seen between the third and fifth year, the rate had dropped approximately to one-third, and when patients were seen for the first time after ten years, a two-year terminal remission had occurred in only 13 per cent. While the overall trends are not surprising, the sharp decline in terminal remissions after the first year of illness is remarkable. It certainly suggests that vigorous anticonvulsant treatment at the onset can prevent chronic seizure disorders. An 85 per cent remission rate is, of course, impressive and one may well be inclined to credit our modern drugs with this result. A look at the literature casts some doubt on this opinion. Table 63, taken

TABLE 63

RELATIONSHIP OF DURATION OF ILLNESS TO SEIZURE CONTROL ACCORDING TO GOWERS, 1885*

	Cases		*Percentage*	
Duration	*Unimproved*	*Arrested*	*Unimproved*	*Arrested*
Less than 1 year	4	19	17	83
1 to 4 years	14	37	27	73
5 to 9 years	9	20	31	69
10 years and over	16	24	40	60
Total	43	100	30	70

*From *Epilepsy and Other Chronic Convulsive Diseases: Their Causes, Symptoms and Treatment* (unaltered republication of the work first published by William Wood and Company in 1885), Dover Publications, Inc., New York, 1964.

from Gowers' book, which was first published in 1885, likewise shows an 83 per cent remission rate for patients who were seen within the first year. The downhill trend thereafter is also observable. His results after the first year are actually better than ours, but Gowers did not define the length of time for which seizures had been "arrested" in his patients. Nevertheless, these results do bring to mind again Hippocrates' statement ". . . it is curable no less than others unless when from length of time it has become confirmed and stronger than the remedies applied." We are therefore dealing with an ancient observation which is very likely to be important for the pathophysiology of epilepsy. There are at least two possibilities that could account for this phenomenon. One is the problem of negative selection as suggested by Margaret Lennox (1967). The later the neurologist sees the patient, the greater the likelihood that the seizure disorder does not respond to the usual anticonvulsant regime. The other possibility is that seizures themselves set up a special condition in the brain which facilitates their recurrence and renders the patient more or less refractory to drug treatment. While the first possibility undoubtedly plays a significant role, this does not necessarily mean that the second possibility should be discarded. Its relative importance cannot be readily evaluated in this country because a vast majority of patients are receiving some treatment very soon after their seizure disorder starts. The problem could and should be studied in one of the underdeveloped nations where regular medical facilities are not uniformly available at the present time.

Lafayette Clinic Outpatient Results

A criticism that could be leveled against the material that has been presented so far is that the patients did not necessarily receive maximum benefit of modern anticonvulsant drugs. It has been mentioned before that the patients' treatment had been carried out by physicians in the community who were usually not specialists in neurology. In order to evaluate the extent to which a neurological training center with special interest in epilepsy can improve seizure patients, we investigated the results

that were achieved by the Neurology Outpatient Department of the Lafayette Clinic. This service was started in January, 1959, and by June, 1966, 123 patients were available who had been followed regularly for periods of time ranging between two and seven years. Patients who had been followed for less than two years were omitted from the study. The previously used criterion of at least three epileptic seizures was again required for a patient to be included in the series. The breakdown in terms of length of treatment is as follows: two years, twenty-seven patients; three years, eighteen patients; four years, twenty-two patients; five years, thirty-two patients; six years, seventeen patients; and seven years, seven patients. The results of treatment

TABLE 64

Last Seizure	Number of Patients
Within 1 month before last clinic visit	71
Within 1 to 3 months before last clinic visit	15
Within 4 to 6 months	5
Within 7 months to 1 year	8
Within 1 to 2 years	9
Within 2 to 3 years	3
Within 3 to 4 years	5
Within 4 to 5 years	3
More than 5 years	4

are listed in Table 64. Fifty-seven per cent of patients had had a seizure within one month of their last clinic visit, and remission of more than six months was accomplished in 32 patients only (26.0%). If we concentrate on the patients who had been seen for at least five years, we find that fifty-six patients qualified and their treatment results are shown in Table 65. Thirty-six patients (64.3%) had had a seizure within the last month of their clinic visit. A terminal remission of at least six months had occurred in eleven patients (19.6%), and a terminal remission of at least two years in only eight patients (14.3%). These are certainly not very encouraging figures, as they are markedly lower than those obtained in the previous follow-up studies at the Michigan Epilepsy Center. It may be argued that the Lafayette

Clinic patients were for the most part treated by resident physicians in training and not by Board certified specialists, which could have influenced the treatment results. This factor was proven not to be decisive, because for a period of one year (July, 1963 to June, 1964) I treated nearly all of these patients myself and was able to render seizure-free only two patients who had previously been uncontrolled.

There are two other arguments that can be advanced to explain the poor treatment results. One is that outpatients may or may not take their medications as prescribed, and the second is

TABLE 65

Last Seizure	Number of Patients
Within 1 month before last clinic visit	36
Within 1 to 3 months before last clinic visit	6
Within 4 to 6 months	3
Within 7 months to 1 year	2
Within 1 to 2 years	1
Within 2 to 3 years	1
Within 3 to 4 years	2
Within 4 to 5 years	1
More than 5 years	4

that we are dealing with a negative selection of patients. Since the Lafayette Clinic is known as a treatment center for epilepsy, the most inveterate cases are likely to come for help. As far as reliability of patients is concerned, seventy patients (56.9%) were judged as reliable, forty-one patients (33.3%) fairly reliable, and only twelve patients (9.8%) were definitely unreliable. This judgment was based on the progress notes which recorded whether patients kept their scheduled appointments and whether they were correct in stating the amount and type of medication that they were supposed to take. While reliability was therefore a problem to varying extents in approximately 43 per cent of the patients, the negative selection of inveterate cases was definitely of importance. Duration of illness and the relationship to terminal remissions are shown in Table 66. Only six patients were seen within one year after onset of the illness,

thirteen patients between two to five years, and thirty-seven patients had had seizures for more than five years. A terminal remission of at least two years had occurred in 21 per cent of the patients that were seen less than five years after onset of seizures, and in 10 per cent of patients who were seen for more than five years after the illness had been present. Although we can see again the relationship between duration of illness and treatment result, the remission rate noted in the group that was seen within the first five years is far from encouraging. A major reason for the poor results is probably the fact that the majority of patients

TABLE 66

Time when patients were first seen after onset of recurrent seizures	*Time of most recent seizure prior to last clinic visit*		
	Less than six months	*Six months to two years*	*More than two years*
1 year or less	3	2	1
2 years	3	0	0
3 years	2	1	1
4 years	2	0	1
5 years	2	0	1
6 to 10 years	11	0	1
11 to 20 years	12	0	2
More than 20 years	10	0	1

who keep attending an outpatient clinic regularly, do so because their seizures are not satisfactorily controlled. Outpatient surveys can therefore not be strictly compared with follow-up results where a group of patients is asked to return regardless of whether the patient appreciates a need for reevaluation or not.

Outpatient reviews really prove only that there still exists a reservoir of epileptic patients who are essentially refractory to our best therapeutic efforts. Although seizures may decrease somewhat in frequency of occurrence or intensity, long-term freedom from seizures is rarely achieved. The size of this reservoir in relation to the total epileptic population cannot be estimated at the present time. This could only be accomplished by a thorough epidemiological survey of a large community.

Lafayette Clinic Inpatient Review

The study on the Lafayette Clinic outpatients demonstrated the existence of this hard-core epilepsy population, but it did not lend itself towards defining the characteristics of the patient who is indeed refractory to treatment. The problem with outpatient evaluations is that one is confronted by two major uncertainties: (1) accuracy of the patient's report about the frequency of his seizures and (2) patient's adherence to his anticonvulsant regime. Both of these problems will inevitably contaminate the results of outpatient treatment. It happens fairly commonly that patients—especially ones with temporal lobe seizures—report that their attacks have stopped when in fact they have merely lost the aura and are no longer aware that seizures are taking place. Reports regarding cessation of petit mal have to be taken with equal caution. Even in regard to grand mal seizures some patients may not be aware of their occurrence, especially if they are predominantly nocturnal. As far as regularity of the patient's medication intake is concerned, one is of course even more at the mercy of the patient's report, which is a most undesirable state of affairs. Routine determinations of serum barbiturate and/or Dilantin levels at the time of each outpatient visit usually are not performed in this country. Both of these uncertainties can be resolved in a hospital situation. Medication intake is controlled by the nursing staff, and seizures are readily observable. We decided to review the charts of all epileptic patients who had been admitted to the inpatient neurology service of the Lafayette Clinic between January, 1959, and July, 1966. Criteria for inclusion in the study were (1) a definite diagnosis of epilepsy as defined previously and (2) a minimum of three weeks of hopitalization. A total of 245 patients became eligible: 132 had been referred from the community because of inadequate seizure control, thirty-one had been admitted from the community because of marked behavioral difficulties, and eighty-two had been referred from the state hospital system of the State of Michigan for research or teaching purposes (57 from Caro State Hospital for Epileptics, 25 from state hospitals for the mentally ill). The charts were abstracted, coded on specially

prepared forms, and the information transferred onto IBM cards. The main goal of the investigation was to define the characteristics of the patient whose seizures persist in the hospital in spite of maximum efforts towards seizure control. Medication regime had been carried out under my personal supervision in each of these cases and all newer anticonvulsants—including experimental drugs (except Tegretol® and Mogadon)—had been used in the treatment of refractory cases. The mean duration of hospitalization was 7.5 weeks. There were 129 males and 116 females in the sample. The mean age was 28.6 years with a range from five to sixty-four years. The mean duration of the illness was fifteen years with a range between one and fifty-two years. The seizure types are shown in Table 67.

TABLE 67

SEIZURE TYPES

Focal grand mal	115
Psychomotor seizures	60
Nonfocal grand mal	59
Focal minor motor seizures	35
Absence	34
Grand mal seizures but history inadequate to differentiate between focal and nonfocal	28
Nonfocal minor motor seizures	21
Focal grand mal variant seizures	15
Akinetic seizures	13
Myoclonic jerks	11
Nonfocal grand mal variant seizures	9
Absences with features of automatisms	8
Absences with some myoclonic activity	8

After obtaining frequency distributions for all variables and eliminating those which were inadequately represented in the sample, the total number of patients was divided into three subgroups: (1) no seizures in the hospital, 118 (48.1%); (2) one to three seizures in the hospital, 47 (19.1%), and (3) more than three seizures during hospitalization, 80 (32.6%).

A sample of the code sheets is contained in the Appendix. The variables that were used for statistical analysis are marked by asterisks. F tests were performed on the continuously distributed variables and Chi Square tests on phenomena that had been

TABLE 68

SIGNIFICANT DIFFERENCES RELATED TO SEIZURE FREQUENCY DURING INPATIENT TREATMENT

	Group I *No Seizures* (*N = 118*)	*Group II* *1–3 Seizures* (*N = 47*)	*Group III* *4 or more Seizures* (*N = 80*)	*F*	*Significance Level* (%)
Frequency of occurrence of seizures just prior to hospitalization	5.2	7.0	8.1	39.1	1
Combination of seizures*	1.8	2.8	3.6	36.9	1
Frequency of maximal occurrence of seizures	6.7	8.3	8.8	29.0	1
Clusters of seizures in one day	1.7	2.0	2.8	26.7	1C
Frequency of injuries during seizures*	1.2	1.4	2.2	26.3	1C
Length of hospitalization in weeks	5.6	8.2	9.7	18.3	1
Seizure patterns in EEG*	1.7	2.3	2.7	14.2	1C
Amount of EEG abnormality*	3.1	3.6	4.0	12.5	1C
Age at onset of recurrent seizures in months	212.0	143.9	117.4	11.2	1
Age at onset of first seizure in months	189.3	124.6	103.3	8.5	1
Amount of abnormality in sleep EEG	2.5	3.1	4.2	8.0	1C
Amount of abortive spike wave activity in EEG	1.1	1.4	1.5	7.5	1C
Amount of schooling	3.7	3.4	2.9	6.0	1

Clusters of seizures over several days, freedom from seizures for several weeks*	1.2	1.3	1.7	6.0	1C
Amount of theta activity in EEG	2.8	2.9	3.3	5.9	1C
Amount of diffuse paroxysmal activity in EEG (not spike wave)	1.0	1.3	1.0	5.8	1C
Age in years	31.4	27.7	25.5	4.8	1
Amplitude of background voltage in EEG	3.4	4.0	3.9	4.8	1
Neurological findings suggesting cerebral pathology	1.6	1.8	2.1	4.5	5C
Duration of main seizure type	7.2	7.7	7.8	4.3	5
Evidence of bilateral cerebral disease	1.8	2.0	2.2	4.2	5
Amount of diffuse delta activity in EEG	1.1	1.1	1.3	4.2	5C
Status epilepticus	1.1	1.2	1.4	4.0	5
Number of admissions	1.2	1.4	1.6	4.0	5
Amount of focal EEG abnormality	1.6	1.6	2.0	3.5	5C
Abortive paroxysmal activity in EEG	1.1	1.2	1.4	3.5	5C
Amount of photic driving response at flash rates of 13 c/s and higher	1.4	1.4	1.1	3.4	5C
Neurotic tendencies on psychological tests	2.5	2.3	2.0	3.2	5C
Immaturity on psychological tests	2.7	3.3	2.1	3.1	5C
Spike wave activity in EEG	1.1	1.2	1.3	3.1	5C
Full Scale IQ	80.8	77.8	72.6	3.0	5

C indicates scales that have been condensed from nine points to four or five points between MEC study (1961) and LC study (1966).

graded as present or absent. Table 68 shows the statistically significant differences between the groups for the F tests and Table 69 for the Chi Square tests. The variables that are marked by asterisks had shown significant differences between the controlled and uncontrolled groups in the second follow-up study conducted at the Michigan Epilepsy Center. The mean values for some of the scales cannot be directly compared with those shown on Table 55 dealing with the results of follow-up at the Michigan Epilepsy Center because by the time of the Lafayette Clinic inpatient review—summer, 1966—we had condensed a number of the nine-point scales to four or five-point scales. The condensed scales are marked by a C on the extreme right hand side of the table. In order to get an approximate comparison between the findings in Table 55 and Table 68, the mean values of the condensed scales would have to be multiplied by two.

Reviewing Tables 68 and 69, we can notice that we are indeed dealing with a continuum of seizure intensity, with Group II standing clearly in the middle on most variables. Patients who had no seizures in the hospital had had, on the average prior to admission, seizures approximately every six weeks; patients with four or more seizures had on the outside approximately one a week. Maximal frequency of seizures in Group I (no seizures in the hospital) was between one and two a month, and in Group III (four or more seizures in the hospital) more than one per week. The Group III patients had more commonly a combination of seizure types; more frequently clusters of seizures in one given day, and clusters of seizures for several days with subsequent freedom from seizures for several weeks; more frequent injuries as a result of seizures; more frequent status epilepticus; were hospitalized longer in an attempt towards better seizure control, and were more frequently readmitted because of poor control after having been discharged from the hospital. They were younger at the time of onset of the recurrent seizure disorder (mean age 9.7 years versus 17.6 years), and younger at the time of first seizure (mean age 8.6 years versus 15.7 years). They had received less schooling, had lower IQs (72.6 versus 80.8), and had more evidence of bilateral cerebral involvement on neurological examination and on the EEG. The electroencephalo-

TABLE 69

SIGNIFICANT DIFFERENCES RELATED TO SEIZURE FREQUENCY DURING INPATIENT TREATMENT

	Group I No Seizures	*Group II 1–3 Seizures*	*Group III 4 or more Seizures*	X^2	*Significance Level (%)*
Nonfocal minor motor seizures					
Absent	117	46	61	34.9	1
Present	1	1	19		
Special schooling					
Absent	92	24	36	27.0	1
Present	19	19	39		
Nonfocal grand mal variant seizures					
Absent	118	47	71	19.2	1
Present	0	0	9		
Theta rhythm present in EEG with eyes open					
Absent	113	44	63	15.9	1
Present	5	3	17		
Akinetic seizures					
Absent	116	46	70	12.2	1
Present	2	1	10		
Psychomotor seizures*					
Absent	100	33	52	10.9	1
Present	18	14	28		
Focal grand mal variant seizure induced by Megimide					
Absent	84	39	52	9.7	1
Present	3	4	12		
Focal response to Megimide in left anterior temporal area					
Absent	89	38	51	9.3	1
Present	3	2	10		
Focal slow wave discharges in resting EEG					
Absent	110	41	64	8.9	5
Present	7	6	16		
Right midtemporal focus in resting EEG					
Absent	114	39	72	8.8	5
Present	4	8	8		

TABLE 69 (Continued)

SIGNIFICANT DIFFERENCES RELATED TO SEIZURE FREQUENCY DURING INPATIENT TREATMENT

	Group I No Seizures	*Group II 1–3 Seizures*	*Group III 4 or more Seizures*	X^2	*Significance Level (%)*
Psychotic symptoms in history					
Absent	84	39	71	8.8	5
Present	33	8	9		
Petit mal absence with myoclonic components					
Absent	118	43	76	8.8	5
Present	0	4	4		
Grand mal but history inadequate to differentiate between focal and nonfocal					
Absent	98	42	77	8.2	5
Present	20	5	3		
Family history of twins on paternal side					
Absent	101	38	69	8.1	5
Present	2	6	4		
Family history of more than one stillbirth					
Absent	99	40	76	7.8	5
Present	6	5	0		
Family history of febrile convulsions on the maternal side					
Absent	98	39	68	7.2	5
Present	2	6	6		
Focal response to Megimide in right midtemporal area					
Absent	85	31	57	7.2	5
Present	8	9	4		
Neurotic symptoms in past history					
Absent	108	39	77	7.0	5
Present	0	8	3		
Family history of early infantile deaths on maternal side					
Absent	97	36	70	6.7	5
Present	8	9	5		

TABLE 69 (Continued)

SIGNIFICANT DIFFERENCES RELATED TO SEIZURE FREQUENCY DURING INPATIENT TREATMENT

	Group I No Seizures	*Group II 1–3 Seizures*	*Group III 4 or more Seizures*	X^2	*Significance Level* (C_c)
Family history of neurological disease other than epilepsy on paternal side					
Absent	96	35	67	6.5	5
Present	8	10	8		
Family history of diabetes on paternal side					
Absent	97	37	67	6.3	5
Present	5	8	9		
Family history of psychiatric disorders on maternal side					
Absent	82	26	58	6.3	5
Present	25	19	18		
Focal minor motor seizures					
Absent	108	38	64	6.2	5
Present	10	9	16		
Family history of febrile convulsions in males					
Absent	97	37	68	6.1	5
Present	4	7	6		
Sleep recording less abnormal than waking record					
Absent	25	8	18	6.0	5
Present	12	5	1		

gram was more abnormal in regard to amount of seizure patterns, general abnormality, amount of theta and delta activity, certain types of paroxysmal discharges and focal abnormalities. The Group III patients also had less of a photic driving response at high flash rates and the sleep recordings were more abnormal. The important negative findings are again: no significant differences in regard to any of the presumed etiological factors. The Chi Square tests demonstrated the seizure types that were the most difficult to control: focal and nonfocal minor motor seizures, nonfocal grand mal variant seizures (major seizures characterized

either by tonic phase only or prolonged clonic without tonic phase —Rodin, 1964), akinetic seizures, psychomotor seizures and petit mal absences with myoclonic features. The seizure type called "grand mal but history inadequate to differentiate between focal and nonfocal" refers mostly to patients with nocturnal seizures. These patients did relatively well in the hospital. The finding that the psychiatric variables of psychotic and neurotic symptoms occurred less frequently in the most severe seizure group does not necessarily indicate an inverse relationship between seizures and these symptoms, but may merely reflect the fact that patients with psychiatric difficulties were admitted on account of this symptomatology rather than because of the intensity of their seizure disorder. The variables dealing with family history are listed in the table because they did show statistically significant differences, but they do not appear to be clinically meaningful at this time and do not form a recognizable pattern. The important feature, as far as family history is concerned, is that family history of epilepsy did not differentiate the groups.

Megimide® activation had been carried out under EEG control in 194 patients, and the induced seizures were photographed in 134 patients. The methodology and preliminary findings have been published previously (Rodin, 1964). The results of Megimide activation were, for the most part, not of importance in regard to the question at hand, except for the fact that focal grand mal variant seizures were more commonly induced in Group III patients, a right midtemporal EEG focus occurred more commonly in Group II, and a left anterior temporal focus was found more commonly in Group III. It is important to point out that although the mean Megimide threshold for seizure induction was the lowest in Group III, the finding did not reach statistical significance. The means were 201 mg for Group I, 203 mg for Group II, and 174 mg for Group III. The standard deviations were 115, 95, and 117 mg respectively. The Megimide threshold does, therefore, not reflect the individual's propensity towards spontaneously recurring seizures, and the drug cannot be used to establish a diagnosis of epilepsy on the basis of the dosage needed to induce a clinical seizure. This finding has also considerable theoretical significance in regard to anticonvulsant

drugs. The pharmaceutical industry depends in its determination of whether a compound has anticonvulsant properties or not, to a large extent, upon changes in threshold to Metrazol® or electrical stimulation. This practice has led to the discovery of important anticonvulsant agents but may not yield the drug which will permanently eradicate the patient's "seizure propensity." Inasmuch as seizure threshold and seizure propensity are different phenomena, different mechanisms are in all probability operative which may well require a different pharmacological attack.

Another important observation from this initial data analysis was that a number of variables which had been found to be of importance in the follow-up study conducted at the Michigan Epilepsy Center—dealing with long-term seizure control—turned out to be important also for the success or failure of short-term anticonvulsant treatment in the hospital.

In this initial data analysis of the Lafayette Clinic inpatient group we had purposely included all epileptic patients, regardless of referring source and regardless of presenting complaint, in order to get the full spectrum of epilepsy. This ranged from mild cases, whose main problem consisted of behavioral difficulties with seizures being more or less incidental, through patients whose seizures could not be adequately controlled on an outpatient basis, to patients who had to reside in an institution for epileptics. It may be argued, however, that by including the institutionalized group we have biased our results and they are therefore not directly applicable to the majority of epileptic patients who reside in the community. Subsequently, in order to meet this criticism, we concentrated in the data analysis on the 132 patients who had been referred from the community because their seizures had not been adequately controlled. The specific question we wanted to answer was— Who is the epileptic patient residing in the community who will continue to have seizures in the hospital even with maximal treatment efforts? The group of 132 patients was therefore split again into three subgroups: one containing sixty patients (45.5%) who did not have any seizures during their entire hospitalization, another containing thirty-four patients (25.7%) who had between one and three

seizures in the hospital, and the third consisting of thirty-eight patients (28.8%) who had four or more seizures while hospitalized. These percentage figures are, of course, of interest by themselves because they indicate that nearly every other patient who is uncontrolled in the community can be brought under temporary control in the hospital environment. This refers however to short-term control only, because it is not justifiable to keep a patient in the hospital for any length of time if he has no seizures. Nevertheless, it is important to point out that a significant short-term improvement can be accomplished in approximately half of the patients who are uncontrolled in their home situation. The thirty-eight patients who had four or more seizures in the hospital are definitely a part of the hard-core group that is essentially resistant to our present day treatment program. F tests and Chi Square tests were again performed in order to find the variables that would distinguish between the three groups. The results of the F tests are listed in Table 70 and the Chi Square results in Table 71. The variables that differentiated the remitted from the unremitted group in the second follow-up study, conducted at the Michigan Epilepsy Center, are marked by an asterisk. The previously mentioned continuum in the severity of seizure disorders is again reflected in the results of treatment. Nearly all variables show an orderly increase in amount of abnormality between the group having no seizures in the hospital and the group having more than four seizures, with the intermediate group standing indeed in the middle. Only amount of paroxysmal activity (not necessarily spike wave) and background voltage of the EEG did not follow this trend. It is again remarkable that none of the supposed etiological factors bears any relationship to result of treatment in the hospital.

If we omit now all those variables that had shown statistically significant differences between groups in one study only, and concentrate on those that had shown statistically significant differences in more than one study, then we find that the prognostic criteria for seizure control which we had set out to develop can be summarized in essentially eight questions:

1. How long has the patient had seizures? The longer

TABLE 70

COMPARISON OF PATIENTS REFERRED FROM THE COMMUNITY FOR SEIZURE CONTROL

	Group I No Seizures (N = 60)	*Group II 1–3 Seizures (N = 34)*	*Group III 4 or more Seizures (N = 38)*	*F*	*Significance Level (%)*
Combination of seizures*	1.8	2.8	3.3	17.0	1
Number of admissions to hospital	1.2	1.2	2.0	12.5	1
Frequency of injuries during seizures*	1.1	1.4	1.9	11.5	1C
Amount of EEG abnormality*	2.9	3.7	4.0	10.4	1C
Length of hospitalization in weeks	4.6	7.8	8.3	9.6	1
Frequency of maximal occurrence of seizures	7.3	8.1	8.8	9.3	1
Frequency of occurrence of seizures just prior to hospitalization	6.7	7.1	8.3	7.6	1
Clusters of seizures over several days, freedom from seizures for several weeks*	1.3	1.4	2.2	7.2	1C
Amount of diffuse paroxysmal activity in EEG (not spike wave)	1.0	1.4	1.0	6.9	1C
Clusters of seizures in one day	1.9	2.0	2.8	6.8	1C
Amount of focal EEG abnormality	1.5	1.6	2.2	6.4	1C
Seizure patterns in EEG*	1.7	2.4	2.7	6.3	1C
Amplitude of background voltage in EEG	3.5	4.3	4.1	4.7	1
Neurological findings suggesting cerebral pathology	1.3	1.6	1.8	4.5	5C
Background amplitude on the left in EEG	3.6	4.3	3.9	4.0	5
Abortive spike wave activity in EEG	1.1	1.4	1.4	3.3	5C
Amount of theta activity in EEG	2.5	2.9	3.1	3.2	5C

C indicates scales that have been condensed from nine points to four or five points between MEC study (1961) and LC study (1966).

TABLE 71

COMPARISON OF PATIENTS REFERRED FROM THE COMMUNITY FOR SEIZURE CONTROL

	Group I No Seizures	*Group II 1–3 Seizures*	*Group III 4 or more Seizures*	X^2	*Significance Level (%)*
Special schooling					
Absent	47	18	20	11.3	1
Present	9	13	17		
Focal slow wave discharges in EEG					
Absent	57	29	27	10.8	1
Present	3	5	11		
Psychomotor seizures*					
Absent	51	24	21	10.4	1
Present	9	10	17		
Nonfocal grand mal variant seizure					
Absent	60	34	34	10.2	1
Present	0	0	4		
Right anterior temporal focus induced by Megimide activation					
Absent	43	28	23	9.8	1
Present	1	0	5		
Right anterior temporal focus in resting EEG					
Absent	55	33	30	6.8	5
Present	5	1	8		
Family history of psychiatric disorder on maternal side of family					
Absent	42	18	26	6.3	5
Present	10	14	8		

the duration of the disorder, the poorer the results of treatment.

2. Is there one seizure type or more than one? The more different seizure types, the less likely it becomes that the patient will be controlled even in a hospital setting.

3. Are psychomotor seizures present? If yes, chances for medical control are immediately markedly reduced.

4. How frequent are the seizures? If they occur several times a month while the patient is on some anticonvulsant medication, chances for complete control are slim.

5. Does the patient have clusters of seizures over a few days and subsequently no seizures for several weeks? The more frequently this phenomenon occurs, the less likely is control achievable.

6. Does the patient injure himself during the seizures? The more frequently this happens, the less likely will he be controlled.

7. What is the degree of abnormality of the EEG while the patient is on some anticonvulsant regime? The more abnormal the EEG, the more likely will be poor control.

8. Are there seizure patterns in the EEG while the patient is on some anticonvulsant medication? The more seizure patterns, the less likely control.

While the presence of one adverse criterion does not rule against success of drug treatment, a combination of a number of these criteria make long-term seizure control unlikely.

Discriminant Function Analysis

After we had established these eight criteria, one could proceed to the next step, namely, determining the precise weights which each of these variables carries in relation to seizure prognosis. The goal of the investigation was to present the physician with a formula, on basis of which he could give a reasonably accurate prediction, whether the seizures are likely to become completely controllable or not. In order to accomplish this aim, a discriminant function analysis was carried out. This is a statistical way of classifying individuals into certain groups and provides the probability of the individual's being a member of any of the groups. The computer program used was an adaptation of the one developed by the University of California (W. J. Dixon, 1965). Up to eleven variables could be used, but the program required complete information on each of the variables. One hundred eight-one Lafayette Clinic inpatients had complete data on all the previously mentioned eight variables. Two subgroups were formed from this material: one consisting of eighty-one patients who had not had any seizures in the hospital while on anticonvulsant medication; the other consisting of one hundred patients who had at least one seizure in spite of adequate

drug treatment. A comparison between the mean values of the two groups on these variables is shown in Table 72. The multiple discriminant function program classified correctly sixty-two (76%) of the patients who did not have seizures in the hospital, and eighty-one (81%) of those who continued to have attacks. The total correct classification was therefore 78 per cent. By chance one would expect a 50 per cent correct classification. Table 73 shows the probabilities supplied by the computer classification in relation to the actual findings at time of hospitaliza-

TABLE 72

	*Group I**	*Group II***
Amount of EEG abnormality	3.1	3.9
Seizure patterns in EEG	1.7	2.6
Psychomotor seizures	1.1	1.3
Combination of seizures	1.8	3.4
Duration of illness	7.2	7.8
Frequency of seizures at present	4.9	7.7
Clusters of seizures over several days, freedom from seizures for several weeks	1.3	1.6
Injuries during seizures	1.3	1.9

* No seizures in hospital
** At least 1 seizure in hospital

tion. It can be seen that if the formula provided a probability of classification that was less than .75, it was not very useful for prognostication. If on the other hand, the probability was .90 or higher, a false classification was encountered only very rarely.

The charts of the three patients whose classifications were grossly in error were then reviewed to ascertain the reasons for the incorrect classification. The patient who did not have seizures in the hospital, in spite of the fact that the formula had predicted with .93 probability that seizures would occur, had been drinking alcohol excessively prior to hospitalization and had neglected her medication regime. The hospital environment provided stability, but after discharge the patient returned to her old ways and the seizure disorder became again uncontrolled. Equally interesting were the two patients who should not have had a seizure in the hospital according to the formula, with a

probability of .93 and .94 respectively, but each one had in fact experienced one seizure while on anticonvulsant medication. In both instances, the seizure occurred in the afternoon of a day when the patients had received an intravenous drug administration in the morning. One patient had received Megimide in an attempt to reproduce his seizure pattern in the EEG laboratory. He had reacted with a marked confusional state which corresponded to his spontaneous attacks, but he did not enter into a generalized seizure. The seizure did occur, as has been

TABLE 73

PROBABILITIES FOR PATIENTS TO FALL INTO GROUP I OR GROUP II

	Correct Classification	*Incorrect Classification*
*Group I**		
Less than .75	16	14
.75 to .89	15	4
.90 to .98	31	1
*Group II***		
Less than .75	27	13
.75 to .89	25	4
.90 to .99	29	2

* No seizures in hospital

** At least 1 seizure in hospital

mentioned, later that afternoon. The other patient had participated in an investigation involving the psychotomimetic properties of Sernyl (1-phenylcyclohexyl piperidine monohydrochloride) in the EEG laboratory during the morning and a generalized seizure occurred on the ward later that afternoon. It is reasonable to assume that seizures would probably not have occurred in these two patients had they not participated in the investigative studies earlier in the day.

Cross Validation

Inasmuch as the variables that had been used for the discriminant function analysis had also shown significant differences between the three groups in the follow-up study at the Michigan

Epilepsy Center (remission for at least two years, seizures improved, seizures same or worse), it was of interest to see what success could be achieved if the formula were to be applied to this independent sample of patients. Fifty-nine patients were available who had complete information on all the eight variables. Nineteen had been seizure free for at least two years, and forty continued to have some seizures. Wherever scales had been changed between the two investigations, the original nine-point scales were condensed to the appropriate Lafayette Clinic scales. The mean values for these two groups of patients on the comparable scales are shown in Table 74. Applying the weights ob-

TABLE 74

	*Group I**	*Group II***
Amount of EEG abnormality	2.8	3.7
Seizure patterns in EEG	1.8	2.8
Psychomotor seizures	1.0	1.3
Combination of seizures	1.6	2.9
Duration of illness	5.6	7.4
Frequency of seizures at present	6.2	7.9
Clusters of seizures over several days, freedom from seizures for several weeks	1.3	1.7
Injuries during seizures	1.8	2.7

* No seizures for at least 2 years

** Seizures within the last 2 years prior to follow-up

tained from the Lafayette Clinic inpatient sample to these fifty-nine patients, it was found that fourteen (73%) of the seizure free and thirty-six (90%) of the other patients were correctly classified. This gave an overall success rate of 84 per cent. The cross validation demonstrated therefore that the formula can be applied with success to another group of patients, and that the weights which predict short-term control can be utilized for prognostication in regard to long-term success of anticonvulsant treatment.

Use of Discriminant Function Formula

Table 75 shows next to each of the eight variables the coefficients for the discriminant functions of Group I and Group II,

as well as the constants that have to be subtracted from the results. In order to arrive at a prediction about the patient's seizure state, the following steps have to be taken:

1. The coefficient next to each variable has to be multiplied by the patient's coded finding on this particular item.

TABLE 75

DISCRIMINANT FUNCTION FOR PREDICTING SEIZURE CONTROL IN THE HOSPITAL

Variables	WEIGHTS *Discriminant Function I*	*Discriminant Function II*
Amount of EEG abnormality	1.57	1.78
Seizure patterns in EEG	0.09	0.21
Psychomotor seizures	6.08	6.25
Duration of illness	2.85	2.92
Frequency of seizures at present	0.56	1.02
Clusters of seizures over several days, freedom from seizures for several weeks	0.77	0.90
Combination of seizures	−0.39	0.06
Frequency of injuries during seizures	−0.41	−0.03
Constant	−17.43	−24.01

2. All eight coefficients are to be added and the constant 17.43 is subtracted. The obtained value represents the discriminant function for the patient's likelihood to fall into Group I (i.e. no seizures in the hospital while on anticonvulsant medication).

3. The original coded findings are then multiplied by the coefficients shown under Discriminant Function II and the constant 24.01 is subtracted from the result. This represents the discriminant function for Group II (i.e. at least some seizures will persist in the hospital in spite of adequate amounts of medication).

4. The patient can be classified in either of the two groups depending upon which discriminant function value is higher.

5. To establish the precise probability with which the patient is likely to fall into the assigned group, the differ-

ence between the two discriminant functions is obtained. If the difference were found to be zero, no prediction would be possible in this particular case. If it were 1.10, the probability for the patient to fall into the higher group would be .75, and if the difference were 4.60, the probability would reach .99. The estimated probabilities of correct classification for all the intermediate values are tabulated in the Appendix.

Two examples might illustrate the use of the formula. For simplicity's sake, those variables that carry a negative sign are grouped together with the constant, which also carries a negative sign, so that the subtotal can be easily subtracted from the values obtained from those variables carrying a positive sign.

EXAMPLE—POOR PROGNOSIS FOR SEIZURE CONTROL

Patient A, DISCRIMINANT FUNCTION 1:

VARIABLE NAME	*WEIGHT*	*CODE AND DEFINITION*	*RESULT*
Amount of EEG abnormality	1.57 × 5	Marked	7.85
Seizure patterns in EEG	0.09 × 4	Very likely but not diagnostic	0.36
Psychomotor seizures	6.08 × 2	Present	12.16
Duration of illness	2.85 × 9	More than 15 years	25.65
Frequency of seizures at present	0.56 × 8	Once a week	4.48
Clusters of seizures over several days, freedom from seizures for several weeks	0.77 × 3	Occasionally	2.31
		SUBTOTAL	52.81
Combination of seizures	−0.39 × 3	Two seizure types	− 1.17
Frequency of injuries during seizures	−0.41 × 4	Injures himself frequently	− 1.64
CONSTANT	−17.43		−17.43
		SUBTOTAL	−20.24
		TOTAL	32.57

DISCRIMINANT FUNCTION I (52.81 minus 20.24 = 32.57)

Patient A, DISCRIMINANT FUNCTION II:

Amount of EEG abnormality	1.78	×	5	Marked	8.90
Seizure patterns in EEG	0.21	×	4	Very likely but not diagnostic	0.84
Psychomotor seizures	6.25	×	2	Present	12.50
Combination of seizures	0.06	×	3	Two seizure types	0.18
Duration of illness	2.92	×	9	More than 15 years	26.28
Frequency of seizures at present	1.02	×	8	Once a week	8.16
Clusters of seizures over several days, freedom from seizures for several weeks	0.90	×	3	Occasionally	2.70
				SUBTOTAL	59.56
Frequency of injuries during seizures	−0.03	×	4	Injures himself frequently	− 0.12
CONSTANT	−24.01				−24.01
				SUBTOTAL	−24.13
				TOTAL	35.43

DISCRIMINANT FUNCTION II (59.56 minus 24.13 = 35.43)
Discriminant Function II (35.43) minus Discriminant Function I (32.57) = 2.86
The probability of the patient falling into Group II is .94.

The final value of 2.86 indicates that the probability of the patient falling into Group II (i.e. continue to have seizures while on adequate amounts of medication in the hospital) is .94. This would be an example for a patient who has a poor prognosis even in the hospital. An example of a patient having a good prognosis for seizure control might be as follows:

EXAMPLE—GOOD PROGNOSIS FOR SEIZURE CONTROL

Patient B, DISCRIMINANT FUNCTION I:

VARIABLE NAME	*WEIGHT*	*CODE AND DEFINITION*	*RESULT*
Amount of EEG abnormality	1.57 ×	1 EEG normal	1.57
Seizure patterns in EEG	0.09 ×	1 Absent	0.09
Psychomotor seizures	6.08 ×	1 Absent	6.08
Duration of illness	2.85 ×	4 Seven to 11 months	11.40

EXAMPLE—GOOD PROGNOSIS FOR SEIZURE CONTROL (*Continued*)

Frequency at present	0.56	×	3	Two to three a year	1.68	
Clusters of seizures over several days, freedom from seizures for several weeks	0.77	×	1	Never	0.77	
				SUBTOTAL	21.59	
Combination of seizures	−0.39	×	1	One type only		− 0.39
Injuries during seizures	−0.41	×	1	Never		− 0.41
CONSTANT	−17.43					−17.43
				SUBTOTAL		−18.23
				TOTAL	3.36	

DISCRIMINANT FUNCTION I (21.59 minus 18.23 = 3.36)

Patient B, DISCRIMINANT FUNCTION II:

Amount of EEG abnormality	1.78	×	1	EEG normal	1.78	
Seizure patterns in EEG	0.21	×	1	Absent	0.21	
Psychomotor seizures	6.25	×	1	Absent	6.25	
Combination of seizures	0.06	×	1	One seizure type only	0.06	
Duration of illness	2.92	×	4	Seven to 11 months	11.68	
Frequency of seizures at present	1.02	×	3	Two to three seizures a year	3.06	
Clusters of seizures over several days, freedom from seizures for several weeks	0.90	×	1	Never	0.90	
				SUBTOTAL	23.94	
Frequency of injuries	−0.03	×	1	Never		− 0.03
CONSTANT	−24.01					−24.01
				SUBTOTAL		−24.04
				TOTAL		− 0.10

DISCRIMINANT FUNCTION II (−24.04 minus 23.94 = −0.10)

Discriminant Function I (3.36) minus Discriminant Function II (−0.10) = 3.26

The probability of the patient falling into Group I (i.e. *no* seizures in the hospital while on anticonvulsant medication is .96.

To save oneself repeated multiplication, a table is included in the Appendix which lists the coefficients for each of the variables on the two discriminant functions in regard to any of the coded scores that can be encountered. It is, of course, obvious that the formula will work only if the same coding system is followed that was used in this study. Duplication of the results will depend not only on the use of the same scales but also on agreement between raters.

"Amount of EEG abnormality" refers to an overall global summary of the EEG findings while the patient is *on* anticonvulsant medication. Representative patterns showing various degrees of abnormalities can be seen in Figures 4–10. The variable called "seizure patterns in EEG" refers to the degree of certainty with which the presence of a seizure disorder can be suspected if the record is read blindly; that is, without access to any information about the patient's clinical condition. The coding of this variable could give rise to some discrepancies between raters who are not trained in the same laboratory.

The following guidelines were used for coding this particular variable. In order to question the presence of a convulsive disorder on reading an EEG blindly, the resting record during the

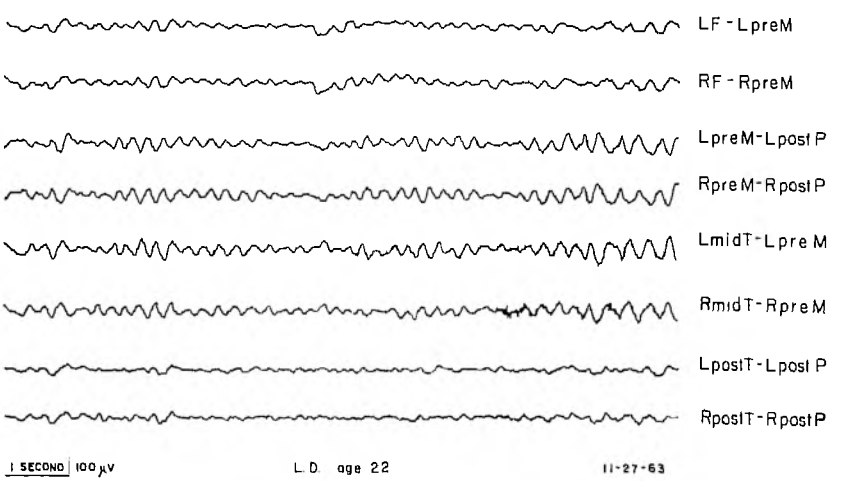


FIGURE 4. Rather stereotyped high voltage 5 c/s background rhythm. Markedly abnormal EEG (Code 5), no seizure patterns (Code 1), no focal abnormality (Code 1).

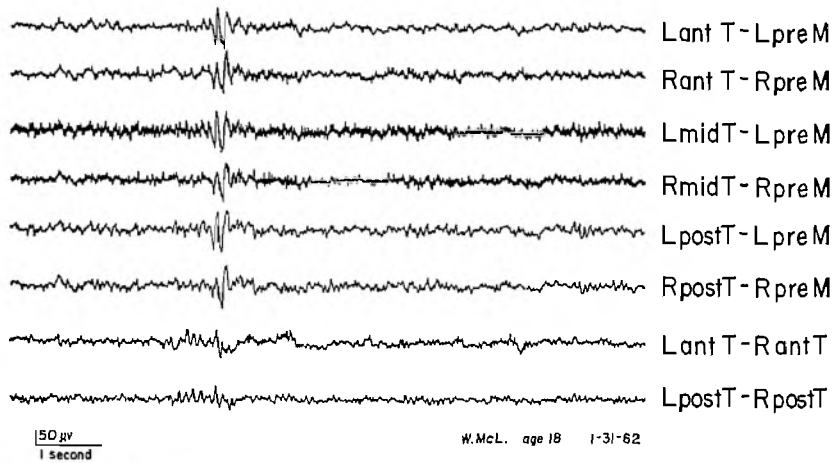


FIGURE 5. Somewhat disorganized background activity, occasional high voltage diffuse bursts but no spike components. Moderately abnormal EEG (Code 4), record raises the question of the presence of a seizure disorder (Code 2), no focal abnormality (Code 1).

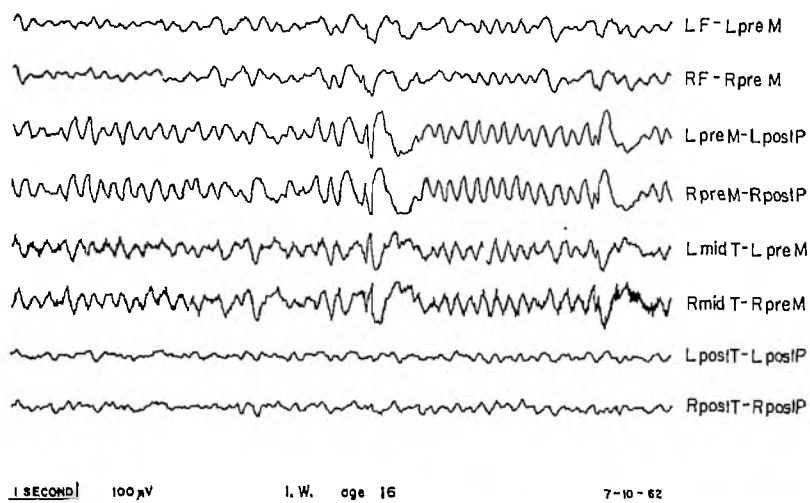


FIGURE 6. High voltage stereotyped 5-6 c/s background rhythm, occasional abortive spike wave activity. Markedly abnormal EEG (Code 5), presence of a seizure disorder is probable (Code 3), no focal abnormality (Code 1).

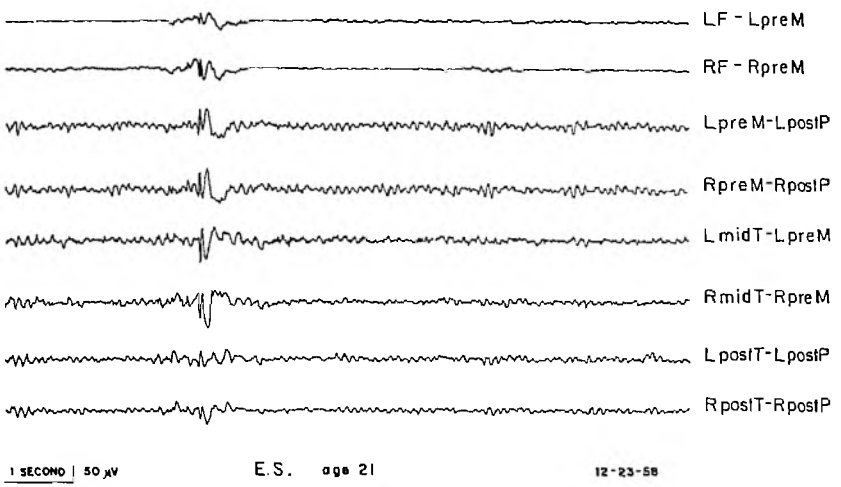


FIGURE 7. Normal background rhythms, occasional isolated spike wave discharges. Moderately abnormal EEG (Code 4), presence of a seizure disorder probable (Code 3), no focal abnormality (Code 1).

waking or sleeping state must have shown at least some diffuse paroxysmal activity with or without low voltage spike components or some focal sharp activity usually in one or both temporal areas. A seizure disorder was regarded as "probable" if there was definite but infrequent spike wave activity, or focal sharp wave or spike activity in any head location (except for occipital location in children where it was relegated to code number two, questionable). Code number four, "very likely but not diagnostic," referred to records which showed frequent brief spike wave bursts or focal sharp wave or spike activity that occurred in a periodic fashion building up in form of a crescendo over a few seconds and then decaying, the phenomenon repeating itself several times during the recording. The record was regarded as "diagnostic" of a convulsive disorder if it showed classical three per second spike wave activity lasting at least four seconds, or if some other clinical and electrographic seizure occurred during the recording period. "Petit mal status" or patterns like those in Figures 11 and 12 were also regarded as being diagnostic of a convulsive disorder. Hypsarhythmia did not occur in this sample of patients but would have been coded as either 4 or 5, de-

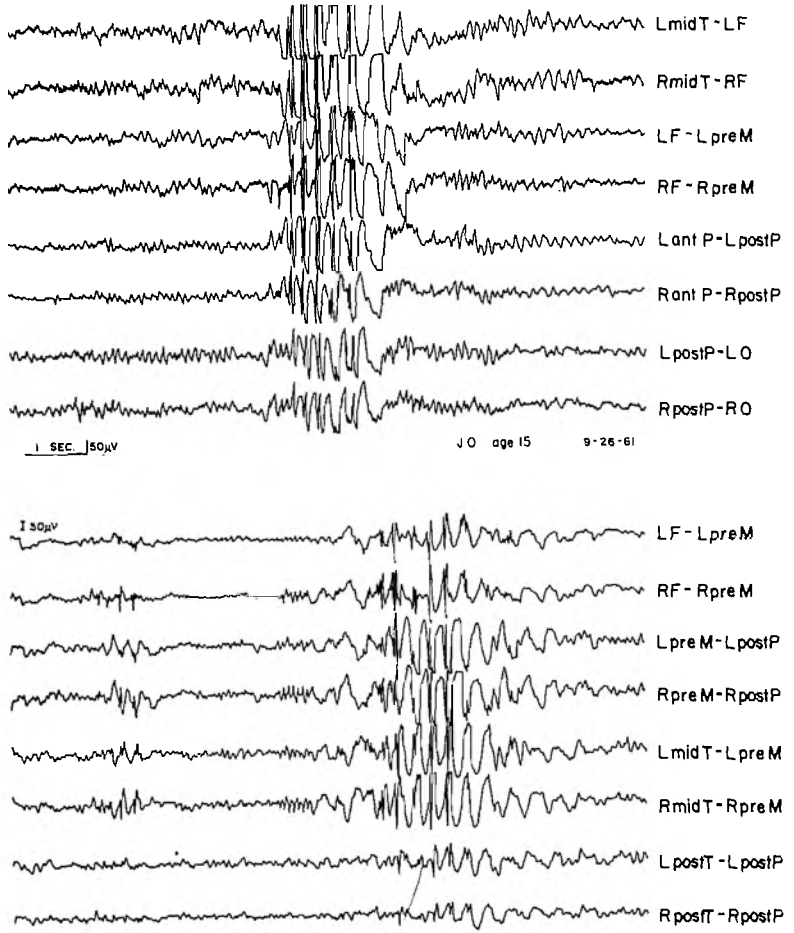


FIGURE 8. Normal background rhythms, high voltage diffuse spike wave discharges lasting 1-2 seconds. During sleep also suggestion of 14 and 6 c/s positive spike activity but the distribution atypical. Markedly abnormal EEG (Code 5), seizure disorder very likely but pattern not diagnostic (Code 4), no focal abnormality (Code 1).

pending on the intensity of the spike components. It should be noted here that the appearance of background activity did not enter into the classification for the variable dealing with seizure patterns. The appearance of the background was taken into account for the overall EEG rating. Likewise, 14 and 6 per second positive spikes were not entered into the "seizure

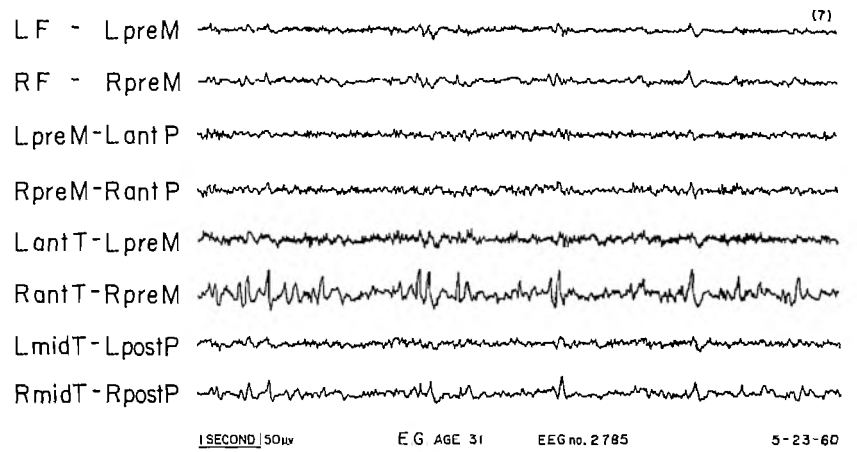


FIGURE 9. Background somewhat disorganized. Marked sharp wave activity in right anterior temporal area. Markedly abnormal EEG (Code 5), seizure disorder very likely but pattern not diagnostic (Code 4), focal abnormality marked (Code 5).

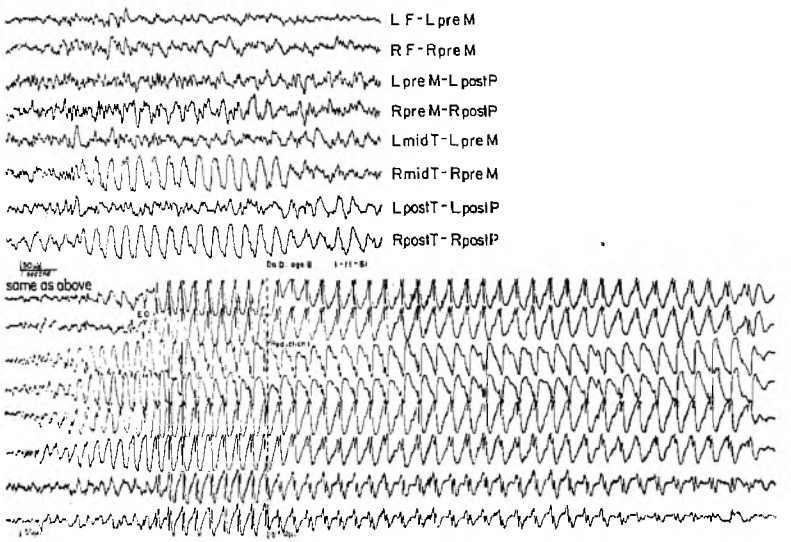


FIGURE 10. Background somewhat disorganized. High voltage rhythmic 2-3 c/s activity in right posterior temporal area spreading to midtemporal region, 3 c/s spike wave activity lasting more than 10 seconds. Markedly abnormal EEG (Code 5), record diagnostic for seizure disorder (Code 5), focal abnormality questionable (Code 2).

pattern" variable, but were taken up in the overall EEG diagnosis, and the record was rated either as borderline or mildly abnormal, depending upon the intensity of the phenomenon. Hyperventilation and photic stimulation had been carried out routinely in all instances. If classical 3 cycles per second spike wave activity lasting at least four seconds was induced with either of these methods, or some other recognized clinical and electrographic seizure, the record was classified as diagnostic for a convulsive disorder. If the resting record had not shown

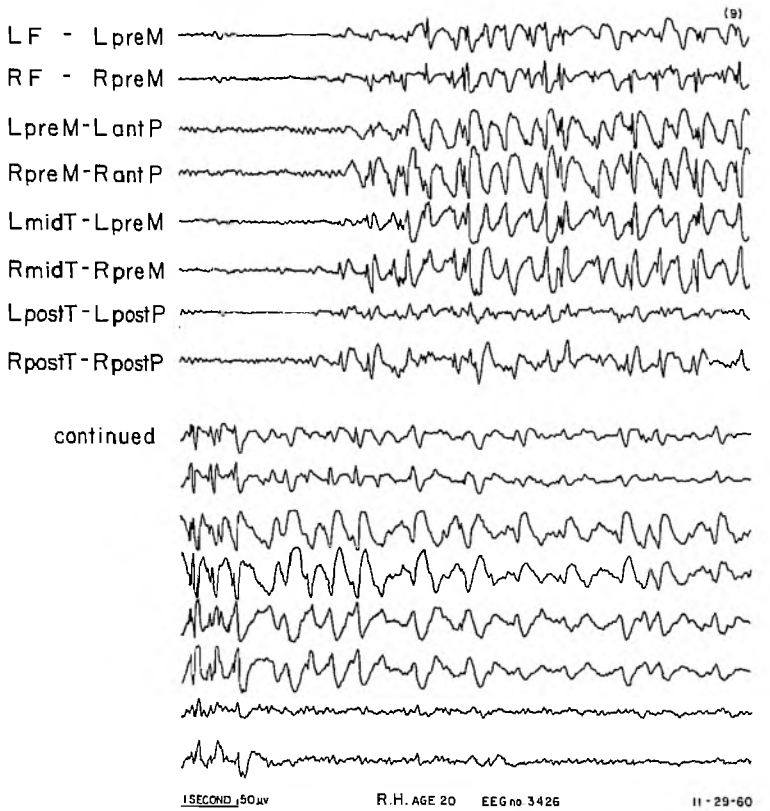


FIGURE 11. Background essentially normal, poorly formed 2-3 c/s spike wave activity lasting somewhat more than 10 seconds. Spike waves more pronounced on the right than on the left, especially in posterior temporal area. Markedly abnormal EEG (Code 5), record diagnostic for seizure disorder (Code 5), focal abnormality questionable (Code 2).

seizure patterns, but the patient responded to the flashing light with brief one to two second episodes of spike wave activity, the variable was coded as questionable or probable, depending upon the intensity of the phenomenon. If myoclonic jerking of the body or extremities accompanied spike wave bursts during photic stimulation, the record was rated either as "probable" or "very likely but not diagnostic," depending upon the intensity of the symptoms.

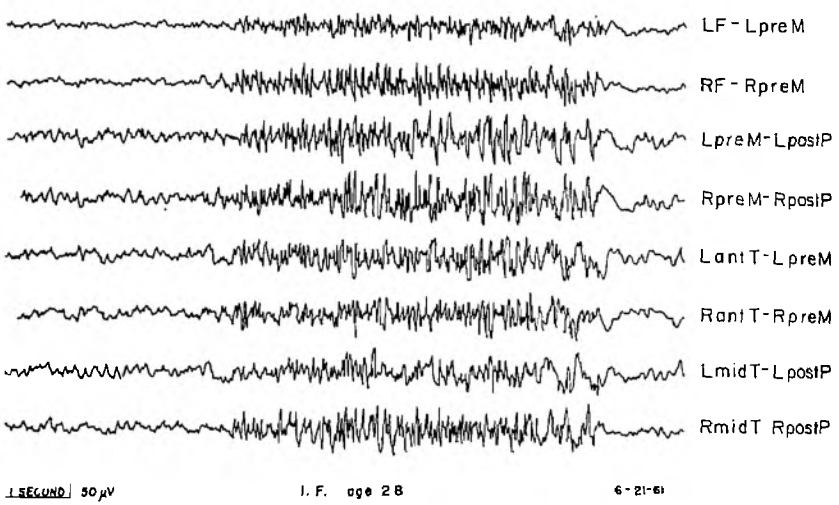


FIGURE 12. Background cannot be evaluated in this section of record because patient somewhat drowsy. Marked diffuse spike activity lasting 5-6 seconds. Example of what has been called grand mal seizure discharge by Gibbs. It should not be confused with barbiturate fast activity. Markedly abnormal EEG (Code 5), record diagnostic for seizure disorder (Code 5), no focal abnormality (Code 1).

It is obvious that there is some judgment involved in coding this particular variable, but differences between competent electroencephalographers are not likely to exceed more than two points. The coefficient for this particular variable is actually the lowest of all eight, and minor variations between raters are therefore not likely to interfere markedly with the predictive value of the total formula.

Psychomotor seizures were rated as either present or absent. "Combination of seizures" was coded on a 1 to 9 scale; 1 mean-

ing: only one seizure type present; 3: two distinct seizure types like grand mal and psychomotor or grand mal and absences; 5: three distinct seizures types, for instance grand mal, absences, and akinetic seizures; 7: four seizure types; and 9: more than four seizure types. The intermediate values (2, 4, 6, and 8) were coded when abortive seizures were also present. If the patient had, for instance, mainly focal grand mal seizures and at times only the aura, code 2 was given rather than 3 because the aura was not regarded as a separate seizure type. Myoclonic jerking, when present in addition to nonfocal grand mal seizures, was also rated as 2 rather than 3. However, if the patient had grand mal seizures and myoclonic seizures, and not merely isolated jerks of an extremity, a rating of 3 was given. A rating of 4 was given, for instance, to a patient who had focal grand mal seizures, intermittent auras and psychomotor seizures. The scale provided, therefore, a rough clinical estimate of epileptogenicity of a patient's brain tissue. Since all seizures have to originate in one restricted area of the brain before they spread to other regions, a variety of seizure patterns indicates that there is, in all probability, more than one cerebral system involved in the genesis of this particular patient's attacks, and one is dealing with a multiplicity of epileptogenic zones.

Duration of illness was coded from the onset of recurrent seizures as defined previously rather than from the very first isolated attacks. The scale went from 1 through 9, and is shown in Figure 13. The scale for frequency of seizures just prior to hospitalization is shown as Figure 14. The variable called "clus-

DURATION OF SEIZURE DISORDER

0	Not Recorded
1	Less than 1 month
2	1–2 months
3	3–6 months
4	7–11 months
5	1–3 years
6	4–6 years
7	7–9 years
8	10–15 years
9	More than 15 years

FIGURE 13.

FREQUENCY OF SEIZURES AT PRESENT

[0] Not recorded
[1] Less than once a year
[2] About once a year
[3] 2–3 seizures a year
[4] 4–6 seizures a year
[5] 7–12 seizures a year
[6] Once a month
[7] 2–3 a month
[8] Once a week
[9] Several a week

FIGURE 14.

ters of seizures for several days, freedom from seizures for several weeks" is a rather interesting one. It was coded on a 1 through 5 scale, and the scale is reproduced as Figure 15. Female patients frequently state that this phenomenon occurs in connection with the menstrual period, but there are any number of male patients who also experience a cyclic occurrence of seizures, and it has been shown in these investigations that it carries a relatively poor prognosis. A detailed investigation of the pathophysiology of this symptom is definitely indicated because it might well shed considerable light on the genesis of epilepsy.

Frequency of injuries was coded on a 5-point scale which is reproduced as Figure 16. It also provides a clinical judgment of the severity of a given seizure. Some patients do not merely crumple and fall to the ground at the onset of the seizure, but pitch violently forward or backward which results in lacerations of supraorbital areas or scalp. The same applies to burn wounds occurring as a result of psychomotor seizures, especially in women working in the kitchen.

CLUSTERS OF SEIZURES OVER SEVERAL DAYS THEN FREEDOM FOR WEEKS

[0] Not recorded
[1] Never
[2] Rarely
[3] Occasionally
[4] Frequently
[5] Usually

FIGURE 15.

If the patient had more than one seizure type, the highest values were used for duration of illness, frequency of occurrence, clusters of seizures, and frequencies of injuries, regardless of whether they referred all to the same seizure type or not. An example might clarify this point. Let us assume a patient had three or four grand mal seizures per year which started ten years ago. These never came in clusters but the patient did, on two occasions, suffer injuries as a result of the grand mal seizures. Five years ago the patient developed psychomotor seizures which occur now at the rate of two to three per month and frequently come in clusters, but the patient has not injured him-

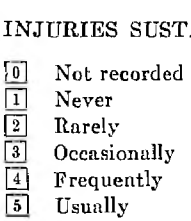


FIGURE 16.

self during these attacks. This particular patient would have received the following codes: psychomotor seizures, 2; combination of seizures, 3; duration of illness, 8; frequency at present, 7; clusters of seizures, 4; and injuries during seizures, 2. Therefore, the codes do not necessarily apply to a given seizure type only but to the patient's overall condition. The reason for doing so lies in the attempt to predict the course of a patient's epilepsy, rather than the course of only one of his seizure types.

Further Cross Validation

After we had demonstrated that the formula which was derived from an inpatient sample could be successfully applied to a group of Michigan Epilepsy Center outpatients followed over at least five years, it was of interest to see what the weights for the eight variables would be if they were developed on the basis of the Michigan Epilepsy Center second follow-up sample. A discriminant function analysis was therefore performed on the fifty-

nine patients who had complete data and the program classified correctly fifteen (79%) of the remitted and thirty-two (80%) of the unremitted patients. The breakdown in regard to probabilities and their accuracy of classification is shown in Table 76. We can see again that classifications involving a probability of less than .75 are not useful for prognostication, but probabilities of .90 or higher are not likely to be in error.

The chart of the patient who was classified by the formula as having had a remission for the past two years with a probability of .93 was reviewed. It was found that this patient was a sixteen-year-old girl at time of initial evaluation who had developed

TABLE 76

PROBABILITIES FOR PATIENTS TO FALL INTO GROUP I OR GROUP II

	Correct Classification	*Incorrect Classification*
*Group I**		
Less than .75	4	3
.75 to .89	2	1
.90 to .99	9	0
*Group II***		
Less than .75	5	6
.75 to .89	1	1
.90 to .99	26	1

* Seizure free for at least 2 years prior to follow-up

** Seizures have occurred within the past 2 years of follow-up

focal grand mal seizures as her only seizure type two years prior to her first visit to MEC. The seizures had occurred several times a week; they had never come in clusters; the patient had never injured herself, and the EEG was normal. She was taking Dilantin (100 mg twice a day) and phenobarbital (32 mg twice a day). After workup at the Center, an increase in her anticonvulsant dosage was recommended. At time of reevaluation the patient was twenty-six years old and continued to have focal grand mal seizures, and at times focal minor seizures several times a month. Her medication regime had never been changed in the past ten years and it still consisted of two capsules of Dilantin

and two 32 mg tablets of phenobarbital. This is obviously an inadequate drug regime and the computer classification is therefore not necessarily in error. This patient did have a good prognosis but her treatment had been neglected.

The coefficients and the constants for classifying patients into the remitted and unremitted group are shown in Table 77. When the weights from Table 77 were applied to the 181 Lafayette Clinic inpatients, one found that fifty-nine (73%) of Group I, and seventy-nine (79%) of the patients of Group II were correctly classified.

TABLE 77

DISCRIMINANT FUNCTION FOR PREDICTING OUT-PATIENT TREATMENT RESULTS

Variables	WEIGHTS *Discriminant Function I*	*Discriminant Function II*
Amount of EEG abnormality	2.46	2.20
Seizure patterns in EEG	0.40	1.36
Psychomotor seizures	9.48	11.37
Duration of illness	1.92	2.60
Frequency of seizures at present	1.35	1.66
Frequency of injuries during seizures	1.25	1.92
Clusters of seizures over several days, freedom from seizures for several weeks	−1.25	−1.57
Combination of seizures	−0.84	−0.27
Constant	−17.81	−30.28

The two samples of patients are of course not identical, and the predictions one is trying to make are therefore not necessarily the same. In the Michigan Epilepsy Center sample, one was trying to predict whether a patient is likely to achieve a terminal remission of his seizure disorder, which had lasted at least two years, after a minimum five-year follow-up. The Lafayette Clinic formula tried to predict whether a patient, when placed in a hospital environment and given adequate amount of anticonvulsant medication, is likely to have seizures during this period of time. One could, therefore, argue that some of the cases that have been classified incorrectly by the formula are not neces-

sarily wrong classifications, but the classification resulted from the different assumptions. It is conceivable, for instance, that a patient who is in the unremitted group, as far as the Michigan Epilepsy Center follow-up is concerned, could have been brought under control had he been hospitalized.

The two formulas together allow different prognostic statements about a given patient and open the way for an interesting experiment. In the future we can classify any epileptic patient by means of both formulas: using the Michigan Epilepsy Center weights to predict whether he is likely to achieve a complete remission with outpatient treatment within the next five years, and using the Lafayette Clinic formula to predict success of treatment in the hospital at this moment. A patient who falls into Group II, on basis of either formula, will probably remain a chronic seizure patient, but if a patient receives a classification of Group II, as far as the outpatient weights are concerned, and a classification of Group I in regard to hospital weights, it would seem that this patient should be hospitalized and short-term control could be achieved which might then lengthen into a long-term remission. This has potential practical importance. If one has a limited number of neurological beds available and a large number of patients on the waiting list, priorities can be established. Those patients who are doing poorly in the community but are classified as Group I on the basis of the Lafayette Clinic formula, could be given preference for admission over the cases that are rated as "poor success likely," even when treated in the hospital.

The results that have been presented so far indicate that the coding system did allow its originator to classify epileptic patients with reasonable accuracy into a potentially controllable or into an uncontrollable group. The question remained whether the system is simple enough that its use can be taught with ease to another physician who is careful in his observations and conscientious in the coding of the data. The material of the second follow-up study of the Michigan Epilepsy Center was coded by myself in conjunction with Doctor N. Velarde, who was at that time a second-year resident in neurology. The material of the Lafayette Clinic inpatients was initially coded by a

second-year medical student, Mr. Richard Robinson. Subsequently, he and I together checked each chart and code sheet for possible errors or differences in judgment. As far as the EEGs were concerned, I had interpreted and coded virtually all of the tracings. There was, therefore, a very definite potential bias in the way the coding forms had been filled out and it remained to be established whether or not another neurologist, using the system alone without interference by me, would come up with essentially similar results.

In 1964, the Michigan Epilepsy Center received a grant from the Division of Vocational Rehabilitation of the U.S. Public Health Service to study the factors that relate to employment problems of epileptic patients. By January, 1967, 236 patients had been seen, and coded, on essentially the same items that were used in the second follow-up study. The neurological evaluations, EEG interpretation, and the coding of the data, were performed by Dr. S. Gonzalez, who had finished his residency training in neurology, had spent one year studying electroencephalography at the same laboratory where my own training had been (Dr. R. G. Bickford, Mayo Clinic) and was on the staff of the Lafayette Clinic and the Michigan Epilepsy Center. This coded material being available, it was of considerable interest to see whether our findings in regard to seizure prognostication would be applicable to this particular group of patients. The sample consisted of adolescents and adults who had been referred to the Michigan Epilepsy Center from a variety of sources (private practitioners, neurologists, schools, social agencies, self-referrals) for this project. A group of 230 patients on whom complete data was available in regard to the eight variables involved in seizure prognosis was then subdivided. Group I consisted of thirty-eight patients who had had no seizures for at least two years; Group II, of 192 patients who had had seizures within the past two years. This was the grouping that had been used for the second follow-up study, except that in the second follow-up study the findings from initial evaluation had been used rather than the findings at follow-up. In the VRA sample only one evaluation was available and these findings had to be used. When the MEC weights that had been derived from the

second follow-up study were applied to the VRA patients, it was found that thirty-four patients of Group I (90%) and one hundred patients of Group II (48%) were correctly classified. The overall success rate was therefore only 58 per cent and not much better than chance. It was then thought that the Michigan Epilepsy Center weights, which had been derived from a relatively small sample of patients (i.e. 59), might not be stable enough to give reliable results. The Lafayette Clinic inpatient weights, which had been derived from a large group of patients were subsequently applied to the VRA sample. This resulted in a correct classification of all thirty-eight (100%) patients of the first group, and of eighty-four (42%) patients of the second group. The overall correct classification had now dropped to 53 per cent. These results presented, of course, a problem. They could be interpreted as follows: (1) The coding system is of no value because another neurologist cannot obtain similar results and (2) the incorrect classification is not really in error but is due to different premises.

Looking at the results in detail, we found it obvious that the distribution of incorrect classification was not one that could be ascribed to chance. The success rate for Group I was 90 and even 100 per cent, depending upon the weights used, but the success rate for Group II was low because too many patients were classified as controlled or controllable. Two possibilities could account for this finding: (1) Dr. Gonzalez had consistently coded the patients lower on the scale items than I had or (2) the VRA group consisted predominantly of patients whose seizure disorders were milder than either of those involved in the second follow-up sample or the Lafayette Clinic inpatient sample.

Looking at the means for the eight variables for Group I and II of the VRA sample, Table 78, we can see that they were indeed, for the most part, lower in the VRA sample than in the previous two groups, (Tables 72, 74). The question remained whether these lower mean values were due to the coding or the properties of the sample. Going over selected charts, we found it obvious that the VRA sample contained, in the great majority, milder cases. This can best be expressed by a comparison of the distribution in regard to frequency of occurrence of seizures

TABLE 78

	Group I	*Group II*
Amount of EEG abnormality	2.7	3.5
Seizure patterns in EEG	1.7	2.4
Psychomotor seizures	1.1	1.3
Combination of seizures	1.9	2.3
Duration of illness	7.5	7.4
Frequency of seizures at present	1.0	5.3
Clusters of seizures over several days, freedom from seizures for several weeks	1.3	1.5
Frequency of injuries during seizures	1.4	1.7

prior to evaluation as shown in Table 79. The incorrect classifications in Group II are therefore not necessarily in error, but they merely state that this particular patient might be brought under control in the hospital or that the patient is likely to have enjoyed a two-year remission five years from now. As a further check on this possibility, two more studies were performed.

Inasmuch as the problem centered around the correct classification of Group II, forty patients were selected from the VRA sample whose seizure frequency matched that of Group II of the second follow-up study. The weights from the second follow-up study were then applied to this group of patients. Thirty-one

TABLE 79

FREQUENCY OF SEIZURES PRIOR TO EVALUATION

Code Number and Description	*MEC 2nd Follow-up (N = 90)* (%)	*LC Inpatients (N = 245)* (%)	*VRA (N = 230)* (%)
1 Less than once a year	2.2	8.2	26.5
2 About once a year	4.4	.4	6.1
3 Two to three seizures a year	7.8	8.9	11.3
4 Four to six seizures a year	6.7	9.4	7.8
5 Seven to 12 seizures a year	11.1	4.1	6.5
6 Once a month	14.4	6.5	8.7
7 Two to three a month	7.8	15.1	10.0
8 Once a week	7.8	7.8	6.5
9 Several a week	37.8	39.6	16.5

(78%) patients were correctly classified as falling into Group II. This is, therefore, virtually the same success rate as had been achieved in the second follow-up project on which the weights had been developed initially (i.e. 80%). This result demonstrated, therefore, that the coding system is indeed useful and can be applied with success by someone else.

It remained to be determined whether the Lafayette Clinic inpatient weights would show a similar success rate when applied to a segment of the VRA population. The second project consisted, therefore, of creating two special subgroups from the total VRA sample: one consisting of sixty-one patients whose seizure frequency had been coded as 1 (i.e. less than once a year); the other of seventy-six patients whose seizure frequency had been coded as 7, 8, or 9 (i.e. between two to three per month to several a week). One would predict that a patient whose seizure frequency on the outside is less than once a year is not likely to have a seizure in the hospital. On the other hand, a patient who has at least two to three seizures per month, might well experience at least one seizure during a three-week period of hospitalization. When the weights from the Lafayette Clinic inpatient sample were applied to these two groups of VRA patients, it was found that sixty-one patients of Group I (100%) and sixty-eight patients from Group II (89%) were correctly classified. These results indicate that the formulas will allow prognostication in regard to a patient's treatment response with reasonable accuracy. They open the door to another practical application in patient management.

The occasion may arise that a patient claims he has not had seizures for the past year in order to obtain, for instance, a driver's license; but the physician has no way of knowing whether the patient's report is accurate or not. One could now compute the discriminant function using the Lafayette Clinic inpatient formula and predict the probability of the accuracy of the patient's statement. If the probability were to be .75 or higher for the patient to have seizures, even in the hospital, it might be advisable to admit this particular patient for observation to the hospital rather than simply accept his word as fact. As has been pointed out earlier, patients may not be aware themselves of

having seizures and underreporting should not automatically be equated with conscious distortion of information.

Two other important points have to be made in regard to the use of the formulas. One is that the weights were derived from a population that was predominantly in the adolescent and adult age bracket. They are, therefore, not necessarily applicable to children. At present we do not have available a sufficient sample of children on whom there is complete information in regard to the mentioned eight variables and who have been followed for a sufficient length of time. It is therefore not possible to determine to what extent the formulas would work in the pediatric age group. This requires further investigation. The second point is that virtually all of the patients had already been on some anticonvulsant regime prior to their being seen either at the Lafayette Clinic or Michigan Epilepsy Center, and the formulas cannot necessarily be successfully applied at this point to patients who have just experienced their first seizure. These aspects of the problem will also require specific investigations in the future.

Chapter 12

PROGNOSIS FOR BEHAVIOR

Having discussed the factors relating to seizure prognosis, we can now turn our attention to the second question that was asked initially, Will the patient's social behavior deteriorate? Here we are, however, on much looser ground than when one is talking about seizures because there are no hard lines that can be drawn. What is acceptable behavior in one family may be unacceptable in another, and there are no suitable quantitative tests that can be applied to a person's social competence. The findings that will be presented in the following pages should be taken as showing general directions, rather than providing specific answers. They are presented in the hope that they will stimulate further research in this area.

At the time of the first follow-up study at the Michigan Epilepsy Center in 1960, we had also inquired of the parents regarding the behavior of the child. For the children living in the community no behavioral difficulties were reported in seventeen instances (62.9%). Mild difficulties were present in five (18.5%), moderate difficulties in four (14.8%) and severe difficulties in one (3.7%). This was in marked contrast to reports of the parents at time of initial evaluation. Only five children (18.5%) had at that time no behavioral difficulties. Behavioral difficulties had been reported to be mild at initial evaluation in eight (29.4%), moderate in eleven (40.7%), and severe in three (11.1%).

Three explanations would seem possible for this phenomenon:

1. Behavior had indeed improved as a result of improvement in the seizure condition.

2. Behavior had improved as a result of normal maturational processes.

3. Behavior had not improved to such a marked extent as suggested by the figures, but the parents had become used to the problem and were able to tolerate more abnormality than they had been able to initially.

The first theory was the easiest to check. Table 80 shows the relationship between seizure state at time of follow-up and behavior. Remission refers to freedom from seizures for two years. It is apparent that reported improvement in the patient's behavior cannot be directly related to the remission of seizures. This leaves us with the other two alternatives, and both of these may well be operative together. The behavioral problems that had been reported initially consisted in the vast majority of

TABLE 80

RELATIONSHIP OF BEHAVIOR TO SEIZURE CONTROL

	Behavior Problem at Follow-up	
Remission	*Yes*	*No*
Yes	4	5
No	6	12

marked temper outbursts, hyperkinetic behavior, and inability to tolerate frustration. These are symptoms that one might well expect to improve with increasing age. Regardless of the causes for improvement in behavior, it was striking to see that only two children had shown deterioration. One had been sixteen months at time of initial evaluation and had developed severe personality difficulties by the time of follow-up. The other had changed from a rating of mild to one of moderate difficulty. The overall trend was quite clearly towards improvement for the majority of the cases.

Although one could expect improvement in most instances, it remained to be determined what type of patient is likely to show continued behavioral difficulties. For this reason it was of interest to look at the statistically significant correlations that were obtained with the variable "behavior at time of follow-up," as

shown in Table 81. Unless when specifically referred to as Evaluation II, the findings deal with observations on first evaluation.

Highest on the list appeared "psychotic tendencies on psychological testing," but it should be emphasized that this particular correlation was based on eight patients only and is undoubtedly inflated by this low number. The table points out that the chronic behavior problems tended to be related to aspects of brain damage and/or intellectual difficulties (e.g. excessively slow EEG background rhythms which persist up to the time of follow-up, excessively high fevers, poor marks in school, grade failure, no formal education, seizure disorder starting during the first year of life, some aspects of focal seizure activity).

The negative findings that are not represented on the table are also worthwhile to point out. One is the absence of a signifi-

TABLE 81

BEHAVIOR PROBLEM AT TIME OF FOLLOW-UP

	r	*Significance Level* (%)
Psychotic tendencies on psychological testing	.945	1
Main background frequency in EEG	−.632	1
Average marks in school	−.619	1
Remission prior to first evaluation	.540	1
Left leg twitching during seizure	.469	1
No formal education	.469	1
Highest fever	.636	2
Grade failure at time of Evaluation II	.517	2
Academic school problem at time of Evaluation II	.478	2
Amount of theta activity in EEG	.407	5
Main background frequency in EEG, Evaluation II	−.403	5
Prognosis for academic achievement	.380	5
Seizures present since first year of life	.357	5
Sitting up age	−.442	10
IQ	−.362	10
Special schooling, Evaluation II	.345	10
Amount of theta activity in EEG, Evaluation II	.344	10
Amount of alpha activity in EEG, Evaluation II	−.321	10
Amount of alpha activity in EEG	−.319	10
Isolated nonfebrile convulsions prior to onset of chronic seizure disorder	.306	10

cant correlation between prognosis for behavior and the actual finding at follow-up. The correlation coefficient was .291. Although this was better than the relationship between seizure prognosis and seizure outcome (.125), it was too low to be of statistical significance. The reason for this finding may lie in the fact that in assigning a prognosis for future behavior I had relied mostly on the description of the child by the psychiatrist in the initial evaluation, and on the social milieu in which the patient was being brought up. These factors turned out to have been quite irrelevant in this sample of patients. The variable "social factors related to present illness" showed a correlation coefficient of .011 with the variable "behavior problem at follow-up" and the variable "psychiatric disorder diagnosed in addition to epilepsy" was correlated —.094 with behavior problems at follow-up. These findings would suggest that as far as epileptic children are concerned, behavior problems tend to persist mainly in the brain-damaged group. Behavioral difficulties as a result of poor social environment can be "outgrown," become internalized, or become tolerated by the parent to an extent that they are no longer reported to the physician. A potentially interesting observation in Table 81 is the finding that a remission in the seizure disorder prior to first evaluation was significantly correlated with subsequent long-standing behavioral problems. This variable refers to a group of children who had a few isolated seizures in infancy but started with chronic recurrent seizures at preschool or school age.

As was mentioned in Chapter 11, a factor analysis was performed on this material and Factor I, Table 82 shows the link

TABLE 82

FACTOR I

.92	Poor marks in school, Evaluation II
.86	Organic pathology suspected on psychological testing, Evaluation I
.57	Low IQ, Evaluation I
.55	Academic school problem at follow-up
.49	Behavior problem at follow-up
.47	Remission of seizures prior to Evaluation I
.39	Academic school problem at time of Evaluation I

between the areas of behavior and intelligence. If the factor is read from the positive side rather than the negative side, it suggests that epileptic children with normal intellect and no evidence of organic pathology on psychological tests, who have not had seizures in infancy (febrile or otherwise), tend to do well in school and are not likely to present chronic behavior problems later on. It should be remembered, however, that these conclusions are based on a small sample of children, and it will be necessary to study another group.

In the second follow-up study, involving ninety patients, we were dealing mostly with an adolescent and adult group of patients and the results will be influenced by this age factor. Sixteen patients (17.8%) had not had any behavioral difficulties at time of initial evaluation. Difficulties were regarded as having been mild in thirty-six (40.0%), moderate in thirty-one (34.4%) and severe in seven (7.8%). At the time of follow-up no behavioral difficulties were reported to have been present in thirty-seven patients (41.1%); problems were regarded as having been mild in twenty-five (27.8%), moderate in twenty-four (26.7%), and severe in four (4.4%). The rating for behavior had remained the same in forty-six patients (51.1%), had improved in forty (44.4%), and had become worse in four patients (4.4%) only. These results are in agreement with the findings obtained at the time of the first follow-up study. The fact that only four (4.4%) patients had shown deterioration in their social functions is reassuring. The changes that had taken place in these four patients were from a rating of mild to one of moderate difficulties. A change from no behavioral problems to one of definite problems had not occurred in this sample. The findings indicate that if an epileptic patient has no behavioral difficulties at the time of initial examination, it is very unlikely that he will develop them later on. The behavioral difficulties apparently tend to appear either prior to the onset of the seizure disorder or at about the same time as the seizures make their appearance. The subsequent course tends to be towards improvement for the majority of patients. Looking at the significant correlates that were obtained with the variable "behavior problem at time of follow-up" in the second MEC follow-up study, Table 83, we find that prognostica-

tion had been easier in this sample than in the group of children.

Social factors had become important now, and an initial diagnosis of psychiatric illness tended to carry a poor prognosis for subsequent behavior. In addition to environmental factors we see, as in the first study, some aspects of brain damage (abnormal neurological examination, abnormal Bender-Gestalt test). The negative signs for the correlations with special schooling and school grades are due to scale construction. Special schooling was coded as 1 (yes) and 2 (no). The scale for average grades went from 1, (unsatisfactory and grade failure) to 9 (superior or honor student). The correlates, although obtained on an adolescent and adult population, point out that the behavioral difficulties are of long standing, going back to school age and possibly in some instances to infancy.

Table 83 contains only those significant correlations that refer

TABLE 83

SIGNIFICANT CORRELATIONS OF FINDINGS OBTAINED AT INITIAL EXAMINATION WITH BEHAVIOR PROBLEM AT TIME OF FOLLOW-UP

	r	*Significance Level* (%)
Prognosis for behavior	.472	1
Prognosis for intellectual functions	.392	1
Social factors contributing to illness	.368	1
Behavioral difficulties in school	.340	1
Objective findings on neurological examination	.292	1
Feeding problems in infancy	.278	2
Attended special school	−.276	2
Amount of schooling	−.272	5
Diagnosis of psychiatric disorder in addition to diagnosis of epilepsy	.267	2
Average marks in school	−.247	5
Prognosis for seizure control	.244	5
"Organic" findings on Bender-Gestalt test	.235	5
Seizures related to menstrual period	.392	10
Frequency of grand mal seizures	.243	10
Grand mal status epilepticus	.224	10
Talking age	.222	10
Duration of pregnancy	.204	10
Spike wave activity in EEG	.200	10

to findings obtained on initial evaluation. The importance of brain damage for the behavior of the patient becomes even clearer if we look at the relationships obtained at follow-up examination, as shown on Table 84. For practical purposes organic mental changes head the list. Most of the other correlates are also associated with this particular problem (deterioration of Performance IQ, concrete proverb interpretations, organic Bender-Gestalt test, recent and remote memory loss, lower Ver-

TABLE 84

SIGNIFICANT CORRELATIONS OF FINDINGS OBTAINED AT FOLLOW-UP EXAMINATION WITH BEHAVIOR PROBLEM AT TIME OF FOLLOW-UP

	r	*Significance Level* (%)
Academic school problem between Evaluation I and Evaluation II	.559	1
Organic mental changes	.542	1
Personality disorder	.430	1
Seizure state at follow-up	.417	1
Unemployed	.383	2
Performance IQ deteriorated between Evaluation I and Evaluation II	.381	5
Proverb interpretations concrete	.365	1
Full Scale IQ	−.363	1
"Organic" features on Bender-Gestalt test	.349	1
Remission for minor seizures	−.348	2
Amount of alpha activity in EEG	−.342	1
Recent memory impaired	.341	1
Response to adequate amount of anticonvulsant medication	−.331	5
Verbal IQ	−.324	2
Number of different seizure types has increased	.321	5
Combination of different seizure types	.316	5
Seizure patterns in EEG	.306	1
Remote memory impaired	.287	2
Serial 7 subtractions impaired	.278	5
Amount of photic driving response at medium flash rates	−.268	2
History of depression	.251	5
Amount of abnormality in EEG	.227	5
Spike wave activity in EEG	.221	5
Sociopathic or antisocial behavior	.221	10
Amount of theta activity in EEG	.204	10
Psychomotor seizures	.195	10

bal IQ, lower Full Scale IQ and difficulties with serial seven subtractions). As far as psychiatric symptoms are concerned, we find mostly personality disorders and depression; sociopathic and/or antisocial behavior are low on the list.

Of definite interest are the correlates with seizure activity, especially the observation of an increase in the number of different seizure types the individual has experienced. The poor response to medication is of course related to the previously mentioned variables, but we do not know what is cause and effect. Do the patients forget or ignore their anticonvulsant regime because of intellectual deficit and/or personality disorders, or do they suffer from a type of seizure disorder which is not responsive to medication? Both factors may be operative to different degrees in different patients. Psychomotor seizures tend to be refractory to medication, especially when they occur in combination with other seizure types. They appear on the table, but they are on the bottom of the list and the correlation does not reach statistical significance. This finding may seem in contradiction to the observations from the factor analysis that were presented in the chapter on prognosis for seizure control. A factor of intractable psychomotor seizures with associated behavioral problems and unemployment had been found. The factor merely states, however, that this group of patients exists and does not necessarily imply that the majority of patients with psychomotor seizures will have significant behavioral problems. It is a well-known clinical observation that a patient who has marked behavioral difficulties, especially if they are of psychotic proportions, is likely to suffer from psychomotor seizures. The converse is, however, not necessarily the case. The diagnosis of psychomotor seizures in a patient does not automatically imply a high degree of probability for the presence of behavioral problems.

Patients who are classified as suffering from psychomotor or temporal lobe seizures do not constitute a homogeneous group. Their seizures may originate in a variety of different structures within the limbic system (e.g. surface of temporal lobe, uncus, amygdala, hippocampus, island of Reil). One could therefore visualize several subgroups of psychomotor seizure patients, depending upon the locus of origin of the seizure discharge. While

a discharging lesion in the hippocampus might give rise to interictal memory loss and confusional states, this would not necessarily be expected from a lesion situated, for instance, in the island of Reil. Rather than taking the position that no statistically significant differences exist in regard to behavioral difficulties between psychomotor seizure patients and other epileptic patients, it would seem more profitable to clearly delineate that subgroup of psychomotor seizure patients in whom behavioral problems are quite prominent, and this aspect of the problem will require further study.

As far as the EEG is concerned, the amount of alpha rhythm at follow-up seems to be correlated best with behavior, a small amount being associated with behavioral difficulties and vice versa. The initial EEG appears to be of no prognostic value for the majority of cases as far as behavior is concerned, but it should be remembered that patterns like hypsarhythmia or petit mal variant were not included in the computations because they did not occur with sufficient frequency in the sample. On the whole we can say that the findings were in much better agreement with the first study than those that had dealt with seizure outcome.

As mentioned in the chapter on seizure prognosis, we were interested not only in intercorrelations but also in significant mean differences between groups. The material was therefore divided into two groups and analysis of variance between groups was carried out. Group I consisted of sixty-one patients with no or slight behavioral difficulties at time of follow-up, and Group II of twenty-eight patients who had shown moderate or marked problems in this respect. The data from one patient with mild behavioral difficulties had been accidentally omitted from the calculations. The 190 variables dealing with findings obtained at initial evaluation that had been used for seizure prognosis were again utilized. Table 85 contains the variables showing significant differences between groups on F tests, and Table 86 shows the Chi Square results. From the asterisks we can notice that all the variables that had shown significant correlations in the correlation matrix are represented in these tables. One of the correlates that had shown a tendency towards statistical significance

TABLE 85

SIGNIFICANT DIFFERENCES BETWEEN GROUPS HAVING BEHAVIORAL DIFFICULTIES AND NO BEHAVIORAL DIFFICULTIES

	No or Mild Behavioral Problem	*Moderate or Marked Behavioral Problem*	*P*	*Significance Level (%)*
Behavior prognosis*	3.8	5.6	19.1	1
Prognosis for intellectual functions*	4.0	5.9	14.5	1
Objective findings of cerebral pathology on neurological examination*	1.6	3.3	14.3	1
Organic findings on psychological tests	3.1	5.1	10.8	1
Seizure state at follow-up*	2.6	4.0	10.3	1
Similarities—Wechsler IQ	9.7	7.0	9.9	1
Average grades in school*	4.2	2.7	8.3	1
Amount of schooling*	4.2	3.2	7.1	1
Social factors contributing to illness*	4.0	5.5	6.7	5
Prognosis for seizure disorder*	4.2	5.2	6.5	5
"Organic" features on Bender-Gestalt test*	3.2	5.0	6.2	5
Talking age	3.9	5.3	6.1	5
Performance IQ	96.6	85.9	5.2	5
Picture Arrangement—Wechsler IQ	9.6	7.7	4.3	5
Duration of individual major seizure	3.5	4.2	4.3	5
Block Design—Wechsler IQ	9.5	7.5	4.2	5
Feeding problems in infancy*	1.5	2.3	4.2	5
Relation of menses to major seizures	3.4	5.6	4.1	10
Comprehension—Wechsler IQ	9.7	7.8	3.8	10
Digit Symbol—Wechsler IQ	8.4	7.0	3.8	10
Full Scale IQ	95.5	86.6	3.4	10
Clusters of minor seizures over several days, freedom from seizures for several weeks	1.6	2.7	3.0	10
Frequency of occurrence of loss of bladder control during major seizures	3.6	4.8	2.8	10

(10% level), namely, seizures occurring mainly around the menstrual period, is again represented as showing a tendency towards statistical significance. This finding might therefore become significant on a larger sample. The correspondence between correlation coefficients and the analysis of variance was again confirmed. Findings which appeared at the 10 per cent level of significance were, however, usually not duplicated by another

TABLE 86

SIGNIFICANT DIFFERENCES BETWEEN GROUPS HAVING BEHAVIORAL DIFFICULTIES AND NO BEHAVIORAL DIFFICULTIES

		No or Mild Behavioral Problem	*Moderate or Marked Behavioral Problem*	X^2	*Significance Level* (C_t)
Behavior problem in school*					
	Absent	57	19	10.0	1
	Present	4	9		
Employed*					
	Yes	18	2	5.8	5
	No	15	11		
Seizures present during first year of life					
	Absent	54	19	5.5	5
	Present	7	9		
Febrile convulsions					
	Absent	52	18	5.0	5
	Present	9	10		
Attended special school*					
	Yes	17	14	4.8	5
	No	42	12		
Postictal headaches					
	Absent	19	16	4.6	5
	Present	29	8		
Family history of excessive nervousness					
	Absent	41	13	4.0	5
	Present	17	14		
Family history of temper outbursts					
	Absent	50	19	3.0	10
	Present	8	8		
SPECIAL TEST FOR STATISTICAL SIGNIFICANCE OF SMALL NUMBERS (FISHER)					
Family history of breathholding spells					
	Absent	53	20		5
	Present	8	7		
Major seizures occurring mostly at night					
	Absent	38	23		5
	Present	10	1		

statistical method and should therefore not be taken too seriously.

In the first follow-up study it was noted that remission of the seizure disorder prior to first evaluation was significantly correlated with behavior problems at time of follow-up. A similar

observation exists in this material. Patients who had febrile convulsions in infancy or childhood showed significantly more behavioral difficulties at time of follow-up than those who did not have this condition. This is an interesting observation which invites further study.

As Tables 85 and 86 show, behavioral difficulties occurred for the most part in patients who had evidence for organic cerebral disease, and/or intellectual problems (objective findings on neurological examination, organic findings on psychological tests, poor school grades, lesser amount of schooling, late onset of talking). It is also of interest to note that the Performance IQ showed significant differences between the two groups, while the Verbal IQ did not. This will be discussed further when our material on intelligence is presented. Furthermore, it should be reemphasized that the behavioral difficulties tended to be of considerable duration going back to school age, and actually may have manifested themselves at times already in infancy in form of feeding problems.

As a next step in the data workup a discriminant function analysis was performed, as had been done in regard to seizure prognosis. Ten variables that had shown significant differences between the groups were selected. Twenty-two patients with no behavioral difficulties at time of follow-up and twenty patients with some problems in this regard had complete data on all the variables. The computer program classified correctly seventeen of the patients who did not have appreciable behavioral difficulties (77.3%), and seventeen who did have behavioral problems (85.0%). The overall correct classification was therefore 80.9 per cent. Table 87 shows the probabilities of the computer classification for Group I and Group II in relation to the actual findings. If the formula gave a .90 or higher probability for the patient to fall into the respective group, there were no incorrect classifications. The variables, with their weights and the constant that has to be subtracted, are shown in Table 88.

In regard to Performance IQ, the actual value was inserted in the formula. The variables "seizures during first year of life," "special schooling," and "behavioral difficulties in school" were rated as 1, meaning absent, and 2, meaning present. Special

TABLE 87

PROBABILITIES FOR PATIENTS TO FALL INTO GROUP I OR GROUP II

	Correct Classification	*Incorrect Classification*
*Group I**		
Less than .75	3	2
.75 to .89	10	3
.90 to .95	4	0
*Group II***		
Less than .75	5	0
.75 to .89	7	3
.90 to .99	5	0

* No or mild behavioral problem.

** Moderate or marked behavioral problem.

schooling had initially carried a negative sign in the coding system, but this was reversed for these computations in order to conform with all the other variables. The variables "organic pathology suspected from psychological tests," "feeding problems in infancy," "social factors contributing to illness," and "objective findings of cerebral pathology" had originally been coded as 1 through 9 scales, but the scales were condensed for

TABLE 88

DISCRIMINANT FUNCTIONS FOR PREDICTING BEHAVIOR

Variables	WEIGHTS *Discriminant Function I*	*Discriminant Function II*
Performance IQ	1.08	1.08
Organic pathology suspected from psychological tests	7.42	7.18
Seizures present during first year of life	19.85	21.27
Behavioral difficulties in school	29.66	33.16
Feeding problems in infancy	5.80	6.67
Talking age	0.08	−0.12
Special schooling	14.50	15.28
Average grades in school	5.91	6.81
Social factors contributing to illness	0.27	0.82
Objective findings of cerebral pathology on neurological examination	6.85	8.72
Constant	−110.17	−122.76

this purpose to 1 through 5 scales (1, meaning no problems; 2, mild difficulties; 3, moderate; 4, marked; and 5, severe difficulties). The scale for "average grades in school" was likewise condensed to a 5-point scale and is shown in Figure 17. The scale for "talking age" is reproduced as Figure 18 and was coded in

AVERAGE GRADES IN SCHOOL

0 Not recorded
1 Unsatisfactory and grade failure
2 Unsatisfactory but no grade failure
3 Average
4 Somewhat above average
5 Superior or honor student

FIGURE 17.

respect to time at which the child started to form the first sentences, rather than in regard to initial utterances like "mama" or "dada."

It is recognized that the weights for the discriminant functions were developed on a small sample, and so far we have not had the opportunity to cross-validate the results on another group of patients. They are presented here, as has been pointed out pre-

TALKING AGE (BEGINNING SENTENCES)

0 Not recorded
1 Under 12 months
2 12–14 months
3 15–17 months
4 18–20 months
5 21–24 months
6 25–28 months
7 29–32 months
8 33–36 months
9 Over 3 years

FIGURE 18.

viously, not as final conclusions but as a basis for further work. They do suggest, however, quite strongly that behavioral difficulties in the epileptic patient are for the most part not primarily due to rejection of the patient by his environment as a result of the seizures. Continued behavioral problems appear to be much more commonly related to aspects of cerebral damage and/or intellectual limitations.

Chapter 13

PROGNOSIS FOR INTELLECTUAL FUNCTIONS

The next question that we had wanted to answer was related to the probability of epileptic patients developing learning difficulties or intellectual deterioration. The average school grades of the twenty-seven children who were involved in the first follow-up project of the Michigan Epilepsy Center and who

TABLE 89

SCHOOL GRADES AT TIME OF FOLLOW-UP

	Number of Children	*Percentages*
Mostly A and B	8	29.6
Mostly C	6	22.2
Mostly D and E	4	14.8
Special education classes	7	25.8
Suspended from school	2	7.4

lived in the community are shown in Table 89. It can be seen that approximately half of the children did have considerable academic difficulties in school. The next table, Table 90, compares the average school grades against seizure state at time of

TABLE 90

SCHOOL GRADES VERSUS SEIZURE STATE

	A	*B*	*C*	*D and E*	*Special Education*	*Suspended*
Still having seizures	2	3	3	3	5	2
In remission	2	1	3	1	2	0

follow-up. No appreciable differences can be noted. Looking, however, at the seizure types of the five unremitted patients who were making A and B grades in school, one found that three had absences with some features of automatic activity as their only seizure type. One patient had psychomotor seizures only, and the other had monthly grand mal seizures.

The variable "learning problems in school at time of follow-up" had been included in the intercorrelation matrix and the statistically significant correlates are shown in Table 91.

Reviewing the table we can see that prognostication had been a great deal easier for school achievement than for seizure con-

TABLE 91

SIGNIFICANT CORRELATIONS WITH LEARNING PROBLEMS IN SCHOOL AT TIME OF FOLLOW-UP

	r	*Significance Level* (%)
Prognosis for academic achievement	.708	1
Organic factors suspected from psychological tests	.619	1
Immaturity on psychological tests	.618	1
Talking age	.603	1
IQ	−.602	1
Behavior problem at follow-up	.478	1
Highest degree of fever	.687	2
Left leg twitching during seizure	.463	2
Amount of theta activity in EEG	.449	2
Objective findings on neurological examination	.427	2
Activity during first year of life	−.743	5 (N = 6)
Personality disturbances on psychological tests	.569	5
Left arm or hand twitching	.415	5
Psychomotor seizures	−.391	5
Focal major seizures	.390	5
Left face twitching	.377	5
Vocalization prior to major seizure	.365	5
Cyanotic during major seizures	.365	5
Seizures present since first year of life	.365	5
Age at time of onset of seizure disorder	−.363	5
Background frequency of EEG	−.411	10
Amount of alpha activity in EEG	−.358	10
Amount of alpha activity in EEG, Evaluation II	−.340	10
Duration of illness	.330	10

trol or behavior. A reasonably accurate prognosis had been made even in the preschool child. We can see again, that similar to the behavior problems, the intellectual handicaps are related to brain damage as expressed by focal motor seizures, objective findings on the initial neurological examination, slow background in the EEG, and long-standing illness. They are not related to a family history of mental retardation. There are several other observations in the table that should be commented upon. Psychomotor seizures were found inversely related to school performance, suggesting that children with this seizure type ought to do well in school. This is, of course, contrary to expectation and may well be the result of the small sample. This question will have to be resolved on another group of patients, but at this point it would be advisable to keep an open mind about the pathological processes underlying psychomotor seizures in children, as these might differ from those of the adult type.

There is one other main problem one would like to have answered, Is the brain damage and resultant IQ loss due to the seizures, or are seizures merely the added complication of preexisting brain damage? Reviewing the table one does not find direct answers to this question, but there are some hints. The fact that the seizures are for the most part focal would argue that brain damage merely facilitated the occurrence of the seizure and was therefore preexisting. However, we also find in the table that cyanosis during the major seizures was significantly correlated with learning problems. One could therefore postulate that these children had suffered more cerebral anoxia during seizures, which had added insult to injury. The same applies to the observation that excessively high temperatures were found positively correlated with learning problems. Temperatures of 105 and 106 degrees Fahrenheit had been reported in some of these children during febrile illnesses and this could have resulted in some added damage to the brain. But we face again the problem that preexisting brain damage could have permitted much more intense seizure activity with resultant obvious cyanosis, and it could also have led to a faulty temperature regulating mechanism, which in turn allowed such excessively high temperatures to occur. A correlation which does not appear in

the table may also be of importance. If seizures per se were the main cause of the learning problems, one might assume that the more frequent the seizures, the more likely learning difficulties occur; but frequency of major seizures was not significantly correlated with this variable. On the other hand one could, of course, also argue that one or two severe seizures lasting one-half hour to one hour may do immeasurably more harm to the brain than any number of major seizures lasting only one to two minutes. These speculations are mentioned here to point out that retrospective studies may not allow final conclusions on this question and a prospective longitudinal approach may be needed. The factor analysis had placed school achievement

TABLE 92

FACTOR I

.92	Poor marks in school, Evaluation II
.86	Organic pathology suspected on psychological testing, Evaluation I
.57	Low IQ on initial psychological examination
.55	Academic school problem at follow-up
.49	Behavior problem at follow-up
.47	Remission of seizures prior to Evaluation I
.39	Academic school problem at time of Evaluation I

mainly in relation to intelligence and "organic" features on psychological tests. The factor did not contain any seizure variables except for a suggestion that some of these patients had isolated convulsions in infancy prior to the start of the recurrent seizure disorder. The factor is listed in Table 92.

SECOND MEC FOLLOW-UP STUDY

As had been mentioned previously, the material of the second follow-up study consisted for the most part of adolescent and adult patients, but the presence or absence of learning problems could be evaluated in twenty-nine patients. Six of the patients had no learning problems at time of follow-up. They were present to a mild degree in three, to a moderate degree in six, to a marked degree in six, and eight patients had experienced severe difficulties in this respect. The statistically significant findings of

the intercorrelation matrix relating learning problems at time of follow-up to findings obtained at initial examination are listed in Table 93. We can note that prognosis for academic achievement showed again a high correlation with actual outcome and that intelligence and aspects of brain damage are the most important variables. Focal seizure activity is represented in the table with only a tendency towards statistical significance (10% level). This suggests that focal seizure activity in the child may have more serious significance for intellectual development than it does when it occurs later in life. The significant correlates between learning problems at time of follow-up and other findings obtained at time of follow-up are shown in Table 94. The table

TABLE 93

SIGNIFICANT CORRELATIONS OF FINDINGS ON INITIAL EXAMINATION WITH LEARNING PROBLEMS IN SCHOOL AT TIME OF FOLLOW-UP

	r	*Significance Level* (%)
Verbal IQ	−.834	1
Full Scale IQ	−.789	1
Prognosis for academic or intellectual achievement	.774	1
Performance IQ	−.677	1
"Organic" findings on Bender-Gestalt test	.614	2
Objective findings on neurological examination	.607	1
Talking age	.604	1
Prognosis for behavior	.599	1
Adequacy of medication regime	−.543	1
Seizures present during first year of life	.539	1
Immaturity on psychological tests	.537	1
Prognosis for seizure control	.528	1
Etiology of seizures unknown	−.463	1
Personality disturbances on psychological tests	.456	5
Attended special school	−.424	5
Duration of seizure disorder	.384	5
Spike wave activity in EEG	−.307	10
Grand mal status epilepticus	.373	10
Behavioral difficulties in school	.350	10
Walking age	.326	10
Focal minor motor seizures	.324	10
Condition of patient's head at birth	.321	10

TABLE 94

SIGNIFICANT CORRELATIONS OF FINDINGS AT FOLLOW-UP EXAMINATION WITH LEARNING PROBLEMS IN SCHOOL AT FOLLOW-UP

	r	*Significance Level* (%)
Amount of schooling	−.919	5
Proverb interpretation concrete	.841	1
Full Scale IQ	−.821	1
Verbal IQ	−.816	1
Organic mental changes	.800	1
Performance IQ	−.723	1
Average grades	−.698	1
"Organic" Bender-Gestalt test	.648	2
Remissions for major seizures	−.614	1
Amount of alpha activity in EEG	−.588	1
Serial 7 subtractions impaired	.577	2
Response to adequate amount of anticonvulsant medications	−.559	5
Behavior problem	.559	1
Remote memory impaired	.551	2
Combination of seizure types	.518	5
Remissions for minor seizures	−.497	5
Recent memory impaired	.475	5
Spike wave activity in EEG	.446	2
Amount of photic driving response at high flash rates in EEG	−.445	2
Amplitude of background rhythms in EEG	−.424	5
Amount of photic driving response at low flash rates in EEG	−.404	5
Sociopathic or antisocial behavior	.448	10
Amount of theta activity in EEG	.352	10
Focal minor motor seizures	.340	10
Seizure patterns in EEG	.312	10

reaffirms the findings in regard to intelligence and organic mental changes, but several additional points emerged that deserve to be mentioned. Verbal IQ seems to be more important for school success than Performance IQ. This is pointed out at this particular time because Performance IQ tends to suffer more in chronic seizure patients than Verbal IQ, as we have heard from Collins (1951), and we will note this to be the case when our IQ material is presented. Presence of seizures during first year of life appeared associated with poor school success in the first and the second follow-up studies, and we are therefore justified in re-

garding this as an important variable in the prognosis for school achievement. It should be emphasized that presence of seizures during first year of life did not correlate significantly with seizure state at follow-up. The importance of a seizure disorder starting during the first year of life lies, therefore, not in the fact that it will necessarily produce hard-core chronic epileptic patients, but that it signals future learning difficulties.

The negative relationship of learning problems with "etiology of seizures unknown" is encouraging because it points out that "idiopathic epilepsy" does not tend to give rise to major learning problems in school. The correlation with adequacy of medication regime carries a negative sign because of scale construction. The correlation states that the children with learning problems had been adequately treated with anticonvulsant medications prior to their first visit to the Center. Their response to anticonvulsants was, however, poor and they did not enjoy appreciable remissions for either major or minor seizures. Other aspects related to seizures were several seizure types in the same patient and spike wave activity in the EEG. The initial EEG showed no useful relationship in this sample; but the follow-up EEG tended to show seizure patterns, low voltage background rhythms, and/or marked theta activity. The correlation of learning problems with a poor photic driving response is of considerable theoretical interest and needs to be investigated further in the future.

Verbal, Performance and Full Scale IQ for Evaluation I, as well as for Evaluation II, had been included in the previously mentioned correlation matrix. The variables that were significantly related to Full Scale IQ on initial as well as follow-up examinations are shown with their correlation coefficients in Table 95. The differences in the magnitude of the correlation coefficients between the IQ at Evaluation I and Evaluation II have to be interpreted with some caution because there are three individuals in each group who had only one Wechsler IQ. The overall trends can nevertheless be discussed. Negative signs refer to low IQ. If we concentrate on the findings that were obtained on initial evaluation and which could have predictive value for IQ level at follow-up, we find mainly those that relate to developmental history, school performance, and findings of a cere-

TABLE 95

SIGNIFICANT CORRELATES WITH FULL SCALE IQ ON INITIAL EXAMINATION AND FOLLOW-UP EXAMINATION

Findings from Initial Examination	*Evaluation I* r	*Evaluation I Significance Level* (%)	*Evaluation II* r	*Evaluation II Significance Level* (%)
Verbal IQ	.934	1	.833	1
Performance IQ	.921	1	.757	1
Academic school problem	−.789	1	−.821	1
Prognosis for academic functions, poor	−.762	1	−.655	1
Bender-Gestalt Test "organic"	−.745	1	−.670	1
Amount of schooling, little	.718	1	.786	1
Average school grades	.556	1	.450	1
Talking age	−.517	1	−.343	2
No special schooling	.491	1	.420	1
Immaturity on psychological tests	−.423	1	−.404	1
Personality disturbances on psychological tests	−.405	1	−.504	1
Prognosis for seizure disorder, poor	−.392	1	−.372	1
Objective findings on neurological examination	−.363	1	−.499	1
Focal minor motor seizures	−.292	5	−.343	1
Birth weight	.289	5	.271	10
Psychotic tendencies on psychological tests	−.286	5	−.319	2
Seizures present during first year of life	−.282	5	−.406	1
Findings from Follow-up Examination				
Full Scale IQ	.858	1		
Verbal IQ	.825	1	.950	1
Performance IQ	.748	1	.913	1
Bender-Gestalt Test "organic"	−.666	1	−.749	1
Organic mental syndrome	−.577	1	−.727	1
Serial 7 subtractions, impaired	−.576	1	−.782	1
Difficulty concentrating	−.376	1	−.478	1
Unemployed	−.366	2	−.330	5
Focal minor motor seizures	−.354	1	−.353	1
Proverb interpretation, concrete	−.305	5	−.473	1
Spike wave activity in EEG	−.264	5	−.225	10

bral deficit on neurological examination and/or the Bender-Gestalt test. These are, of course, correlates that one expects on general grounds regardless of the presence or absence of epilepsy.

As far as specific correlates of Full Scale IQ at Evaluation I with epilepsy variables are concerned, these are quite meager: we find only focal minor motor seizures and presence of seizures during the first year of life. Seizure frequency, duration of the seizure disorder, and most important, seizure outcome at the time of follow-up, were not significantly correlated with initial IQ. The correlate with seizures during the first year of life is of interest from various points of view. It could be argued that seizures and the low IQ arise from a common denominator, namely prenatal or perinatal brain damage. Clinical experience indicates that this is certainly the case in a considerable number of instances, but it is of interest that the Full Scale IQ did not correlate significantly with the variable "etiological factors in neurological history." This suggests that the presence of known injuries to the central nervous system did not suppress the IQ too markedly in some cases and in other instances of markedly depressed IQ, no etiology was present by history. A detailed investigation was now required in regard to the relationship between age at time of onset of the seizure disorder and intellectual deficits. Before we go into this problem, there is other material that should be looked at. A number of significant correlations were present with the IQ as measured by the time of follow-up and not with initial IQ. These are listed in Table 96. The variables that were obtained on initial evaluation appear in the upper half and those that were obtained at follow-up, in the lower half of the table. Of interest is the fact that duration of seizure disorder at Evaluation I was correlated significantly with IQ at Evaluation II, but not with IQ at Evaluation I. This might suggest that a long-standing seizure disorder could have, by itself, a deteriorating effect on the IQ. Spike wave activity in the EEG also seems to carry a poorer prognosis for intellectual functions. The finding that isolated seizures in childhood tend to be associated with a poor prognosis, not only for behavior but also for intelligence, invites further study.

The intercorrelation matrix also had contained, in addition to Full Scale IQ, the Verbal and Performance IQ scores. It was thereby hoped to get a somewhat more detailed appraisal of relationships between clinical findings and cognitive functions.

A comparison of the correlation coefficients for Verbal, Performance, and Full Scale scores obtained at time of follow-up is presented in Table 97. Only those variables are shown that were found correlated to a statistically significant degree with either the Verbal or Performance scales. Variables that correlated with Full Scale IQ only, were omitted. All variables refer to findings obtained at initial evaluation. The variables are arranged from highest to lowest correlation coefficient for the Performance IQ.

TABLE 96

ADDITIONAL SIGNIFICANT CORRELATIONS OBTAINED WITH FULL SCALE IQ AT TIME OF FOLLOW-UP

Findings from Initial Examination	*r*	*Significance Level* (%)
Spike wave activity in EEG	−.388	1
Isolated infantile nonfebrile convulsions	−.327	1
Personal relationships during adolescence	.341	2
Prognosis for behavior	−.328	1
Duration of seizure disorder	−.292	5
History of bedwetting	.275	5
Etiology of seizure disorder unknown	.267	5
Findings from Follow-up Examination		
Remote memory	−.374	1
Behavior problem	−.363	1
Overall condition of patient	−.333	1
Amount of EEG abnormality	−.314	2
Amount of alpha activity in EEG	.263	5

It can be seen that the variables dealing with seizures (seizures present during first year of life, focal minor motor seizures, duration of seizure disorder, spike wave activity in EEG) were all correlated to a higher degree with Performance than with Verbal IQ. Findings on the neurological examination and the Bender-Gestalt test related also more to the Performance score than the Verbal, but school achievement was tied closer to the Verbal than the Performance areas.

The statistically significant correlations between the Verbal,

TABLE 97

SIGNIFICANT CORRELATIONS BETWEEN WECHSLER IQ VARIABLES AND FINDINGS OBTAINED ON INITIAL EXAMINATION

	Verbal	*SL** (%)	*Performance*	*SL** (%)	*Full Scale*	*SL** (%)
Performance IQ	.642	1	.779	1	.757	1
Full Scale IQ	.825	1	.748	1	.858	1
Bender-Gestalt Test "organic"	−.580	1	−.657	1	−.670	1
Amount of schooling	.813	1	.630	1	.786	1
Verbal IQ	.886	1	.609	1	.833	1
Prognosis for academic achievement	−.623	1	−.593	1	−.655	1
Objective findings on neurological examination	−.431	1	−.529	1	−.499	1
Personality disturbance on psychological tests	−.490	1	−.438	1	−.504	1
Seizures present during first year of life	−.356	1	−.476	1	−.406	1
Did not attend special school	.400	1	.398	1	.420	1
Spike wave activity in EEG	−.339	2	−.386	1	−.388	1
Personal relationships during adolescence	.284	5	.357	1	.341	2
Focal minor motor seizures	−.299	2	−.349	1	−.343	1
Immaturity on psychological tests	−.389	1	−.348	1	−.404	1
Prognosis for seizure disorder	−.370	1	−.320	2	−.372	1
Duration of seizure disorder	−.246	10	−.314	2	−.292	5
Isolated nonfebrile convulsions in infancy	−.304	2	−.305	2	−.327	1
Sitting up age			−.303	5	−.250	10
Birth weight			.302	5		
Average grades in school	.512	1	.290	5	.450	1
Talking age	−.349	2	−.287	5	−.343	2
Prognosis for behavior	−.321	2	−.285	5	−.328	1
Etiology of seizures unknown	.254	5	.244	10	.267	5
History of bedwetting	.268	5	.240	10	.275	5
Psychotic tendencies on psychological tests	−.344	1	−.224	10		
Family history of infantile nonfebrile convulsions	.255	5				

* Significance Level

Performance, and Full Scale IQ obtained at Evaluation II with clinical findings at time of follow-up are shown in Table 98. The variables are arranged from highest to lowest correlation co-

TABLE 98

SIGNIFICANT CORRELATIONS BETWEEN WECHSLER IQ VARIABLES AND FINDINGS OBTAINED ON FOLLOW-UP EXAMINATION

	Verbal	*SL** (%)	*Perform-ance*	*SL** (%)	*Full Scale*	*SL** (%)
Bender-Gestalt Test "organic"	−.075	1	−.737	1	−.749	1
Academic school problems	−.816	1	−.723	1	−.821	1
Organic mental changes	−.658	1	−.695	1	−.727	1
Serial 7 Subtractions impaired	−.743	1	−.657	1	−.782	1
Difficulty concentrating	−.443	1	−.424	1	−.478	1
Proverb interpretation concrete	−.476	1	−.371	2	−.473	1
Amount of EEG abnormality	−.235	10	−.363	1	−.314	2
Behavior problem	−.324	2	−.361	1	−.363	1
Focal minor motor seizures	−.313	2	−.355	1	−.353	1
Amount of alpha activity in EEG			.297	2	.263	5
Amount of photic driving at high flash rates in EEG			.272	5		
Amount of photic driving at low flash rates in EEG			.268	5		
Overall condition of patient	−.350	1	−.262	5	−.333	1
Amount of fast activity in EEG			−.253	5	−.234	10
Remote memory impaired	−.421	1	−.240	10	−.374	1
Recent memory impaired			−.227	10	−.313	2

* Significance Level

efficient for the Performance IQ. These findings agree with those shown in the previous table but point out in addition that the EEG appears more closely related to the Performance than to the Verbal areas.

IQ Change in Relation to Seizure State

The results presented so far do not allow a direct differentiation between patients who had a low IQ possibly even before the onset of their seizure disorder and patients whose IQ had shown some decrease as a concomitant of the illness. A comparison of initial against follow-up Wechsler IQ scores was possible in 56 patients. Table 99 shows the mean values for the Full Scale,

TABLE 99

MEAN WECHSLER IQ LEVELS FOR INITIAL AND FOLLOW-UP EXAMINATION
(N = 56)

	Evaluation I	*Evaluation II*	*Difference*	*t*	*Significance Level (%)*
Verbal	94.50	93.67	− .82	0.72	NS
Performance	95.75	91.82	−3.92	2.75	1
Full Scale	94.96	92.41	−2.55	2.16	5
Information	8.19	8.58	+0.39	1.68	NS
Comprehension	9.40	9.33	−0.07	0.20	NS
Arithmetic	8.06	9.22	+1.16	2.96	1
Similarities	9.25	9.63	−0.38	1.01	NS
Digit Span	8.67	8.67	0.00	0.00	NS
Vocabulary	8.50	8.19	−0.30	1.09	NS
Digit Symbol	8.33	7.51	−0.82	2.60	5
Picture Completion	9.03	9.78	+0.75	2.20	5
Picture Arrangement	9.90	8.45	−1.45	3.39	1
Block Design	9.55	9.05	−0.50	1.58	NS
Object Assembly	9.98	8.12	−1.85	4.28	1

NS = not significant

Verbal, and Performance IQs as well as for subsections of the Wechsler tests on the patients involved in the second follow-up study. The differences between first and second evaluation, and the results of the t test for nonindependent means and levels of statistical significance are also shown. The IQ levels are somewhat biased towards the higher end because patients with marked mental retardation did not receive a Wechsler test on initial evaluation. We can see that at initial, as well as follow-up, examination the IQ was within the normal range, but by the

time of follow-up it had definitely shifted towards the low normal end. We can also note that the Verbal and the Performance IQ tended to show independent behavior. The Performance IQ dropped by nearly four points while the Verbal IQ showed a mean drop of less than one point. Within the verbal area an actual increase had taken place in the Arithmetic subsection. The Performance subtests which showed the most marked decrease were Object Assembly, Picture Arrangement, and Digit Symbol. One Performance subtest, namely, Picture Completion had shown some improvement. These observations indicate that there is indeed a slight but statistically significant overall decrease in intellectual functions present when patients are retested after a period of several years. The mean decrease is so slight that it would not be discovered by interview techniques and the patients remain within the "normal" range of intelligence. The fact that the performance items of the Wechsler test suffered the most is important to recognize, because deficits in these areas will surely be missed if one relies on one's judgment of the patient's intelligence on an interview only. With the verbal functions remaining intact, the patient may well be able to hide his performance deficit and the physician may remain unaware that some deterioration has taken place in the patient.

Analysis of Variance

Although the findings that have been reported indicated that intellectual deterioration does take place in a number of instances, they do not allow precise statements in regard to the question, Who is the epileptic patient whose IQ will deteriorate, as opposed to the patient whose IQ will stay intact or even increase? Theoretically it would be desirable to compare an equal number of patients, preferably fifty or more, whose IQ had increased by ten points or more, with an equal number whose IQ had remained within ten points in either the upward or downward direction, and an equal number of patients who had deteriorated ten points or more. This theoretical ideal could not be reached in our study because we had only fifty-six patients who had two Wechsler IQ tests. Patients who had received the

Stanford-Binet test during the initial evaluation could not be used for comparison. The Full Scale IQ had deteriorated ten or more points in eleven patients and had increased by ten or more points in five. Looking at the subtests, we find a decrease of ten or more points had occurred in the verbal area eight times and in the performance area, fourteen times. An increase of ten or more points had occurred in the verbal area also eight times and in the performance area five times. These observations show also that the performance area is more frequently involved in deterioration and is less likely to improve than the verbal skills.

We were confronted with the fact that a definitive conclusion about the clinical characteristics of the patient who will in all likelihood deteriorate in his intellectual functions may not be possible to accomplish in view of the small sample available; therefore, a compromise solution was attempted. The group of fifty-six patients who had had two Wechsler IQ tests was split into two subgroups. One consisted of patients whose Full Scale IQ had dropped by seven points or more, and the other consisted of patients who had either lost up to six points only, had remained the same, or had shown an increase by any number of points. Patients with initial IQs of 70 or below were excluded in order to avoid contamination of the sample with mental deficiency. This left twenty-two patients whose IQ had dropped seven points or more and eighteen patients who had shown less drop or an increase. The groups were then subjected to the same analysis of variance procedures that had been applied to seizure state and behavior. The variables which showed significant differences between the groups are listed in Table 100. The most important aspect of this table is the observation that seizures per se were indeed related to a deterioration of the IQ. The deterioration was unrelated to presumed etiology or the presence of damage to the central nervous sytem. It occurred more commonly in patients who had initially no or little evidence of organic dysfunction on the Bender-Gestalt test. The most surprising finding was that it occurred mostly in patients who had an initially higher IQ.

We have mentioned previously in the literature review that epileptic patients as a group tend to have a mean IQ that is

TABLE 100

INITIAL EXAMINATION FINDINGS RELATED TO SUBSEQUENT CHANGE IN WECHSLER IQ SCORES

FULL SCALE IQ

	Decreased 7 or more points (N = 22)	*Decreased less, remained same, or increased* (N = 18)	*F*	*Significance Level* (%)
Performance IQ	108.3	99.2	11.5	1
Full Scale IQ	108.3	99.1	10.9	1
Present seizure state	4.0	2.2	9.3	1
Combination of seizures	2.7	1.7	9.3	1
Block Design—Wechsler IQ	11.8	9.6	8.5	1
Object Assembly—Wechsler IQ	12.2	10.3	7.6	1
Overall condition of patient	4.4	2.9	6.5	5
Relationship of time of day to minor seizures	1.3	3.7	6.2	5
Social factors contributing to illness	5.2	3.5	5.5	5
Frequency of occurrence of major seizures at initial evaluation	6.8	5.0	5.2	5
Organic features on Bender-Gestalt Test	1.5	2.6	4.7	5
Immaturity on psychological tests	5.1	6.3	4.5	5
Behavior problem on follow-up	3.1	1.9	4.5	5
Duration of seizure disorder (minor seizures)	7.0	5.2	4.3	5
Verbal IQ	105.8	98.8	4.3	5
Amplitude of background rhythms in EEG	5.1	6.3	4.1	5

within the "normal" range, but it is shifted towards the lower end of this range. The phenomenon demonstrated here would account for this observation. The higher IQ patients in the "bright normal" or "superior" range may suffer most from the influence of seizures and slip down into the "normal" group. Although they are now, technically speaking, normal, a real loss has taken place. It is conceivable that this loss in mental acuity is experienced by the patient and reacted to by various mental mechanisms leading to overt psychiatric symptoms, which differ between persons and depend, at least in part, upon the basic

personality structure of the individual. These symptoms could then express themselves clinically as personality disorders, depression, or withdrawal. This theory does not apply to epilepsy only; it could also be applied to other "degenerative" conditions of grey matter. It links the areas of psychiatry and neurology and suggests that, prior to the overt neurological disorder, a number of patients with beginning intellectual loss may have to move through the stage of "psychiatric illness' because their organic defect is too mild to be detected by everyday clinical practice.

To reemphasize this point it can be stated: The fact that a "normal" IQ is measured in a patient does not mean that it could not have been higher prior to the illness. There exists an electroencephalographic corollary to this theory. A low voltage desynchronized EEG does not necessarily mean that this particular tracing is normal for the patient; it could have changed from a dominant alpha pattern to the low voltage desynchronized type of activity. Low voltage desynchronized records have to be interpreted as normal because they occur quite commonly in normal individuals; however, these records may not represent the usual EEG of the person but a deterioration from a better organized alpha pattern. Our concepts of "normality" in the clinical, as well as the electroencephalographic field, will have to undergo a rather critical reassessment in the future.

Returning to epilepsy and the data on hand, we should emphasize that this deterioration from a higher level is not necessarily permanent, but reflects the state of affairs at a given moment in time. The work carried out on serial IQ tests in the 1930s and early 1940s becomes therefore most important because it emphasized the fluctuations that can occur in the IQ over relatively short periods and these fluctuations were not necessarily tied to the seizure state of the patient. The test-retest intervals reported in the literature were for the most part relatively short. One could conceive, however, of two processes being operative in the epileptic patient. One would consist of short-term, relatively marked fluctuations in IQ in upward or downward direction, depending in part upon the time relation to the patient's last seizure; the other, a long-term, less marked

downward course, if the illness persists unchecked for several decades. The short-term fluctuations are important to remember because they are quite likely to tie in with the emotional functions of the individual. The patient being deprived of a relatively stable internal environment, it is probably very difficult, if not impossible, for him to maintain a normal balance in his emotional life.

One other potentially important relationship to IQ deterioration mentioned in the table has still to be mentioned: the finding that adverse social factors were significantly more common in the deteriorating group. We are again confronted here with the problem of what is cause and what is effect. It could be theorized that a disrupted home life has a direct influence on the patient's intellectual functions. But it seems more likely that the relationship is indirect. A disturbed social environment is likely to lead to increased chronic stress on the patient, which leads to poor seizure control and subsequent intellectual loss. We are, however, at this point exceeding our data and should return to the facts as they were observed.

It was mentioned in the literature that the fluctuations in the patient's IQ could not be related to the current seizure state of the patient. The IQ may go up and the seizures become worse or vice versa. Let us look at our data in this respect. Three tables were prepared to allow easy comparison of the findings. Table 101 lists the patients whose Full Scale IQ had increased. The patients are arranged from most marked to least marked increase in Full Scale IQ points. Table 102 shows the patients whose Full Scale IQ had either shown no change or a mild decrease of up to and including six points. Table 103 shows the patients whose Full Scale IQ had dropped by seven or more points. The code for the numbers under seizure state at follow-up examination is shown in Table 104.

There was not a single patient in the entire sample whose seizure state had been rated as 9 at follow-up. The worst outcome was a rating of 8 which had been given to one case only. The tables demonstrate not only the relationship of seizure outcome to IQ change, but also the relative movement of Verbal versus Performance IQs, and the actual IQ values that were obtained on

the two evaluations. Looking at seizure state and IQ change first, we find an impressive correspondence if we concentrate on the group that had been seizure free for two years or more. Of the twenty patients whose IQs had increased, twelve were seizure free (60%). Of the fifteen patients whose IQs had shown no change or slight decrease, four (26.6%) were seizure free, and of the twenty-one patients whose IQs had decreased seven or

TABLE 101

RELATIONSHIP OF IQ CHANGE TO SEIZURE STATE AT FOLLOW-UP: IQ POINTS INCREASED

Patient Number	*Verbal*			*Performance*			*Full Scale*			*Seizure State*
	I	*II*		*I*	*II*		*I*	*II*		
360	90	101	(+11)	93	119	(+26)	91	109	(+18)	3
332	57	75	(+18)	54	58	(+ 4)	51	66	(+15)	3
173	83	94	(+11)	69	76	(+ 7)	74	86	(+12)	1
340	91	101	(+10)	100	114	(+14)	95	107	(+12)	1
328	66	65	(− 1)	48	72	(+24)	54	65	(+11)	3
392	99	110	(+11)	99	104	(+ 5)	99	108	(+ 9)	1
283	119	139	(+20)	97	92	(− 5)	109	118	(+ 9)	1
48	103	107	(+ 4)	85	95	(+10)	94	102	(+ 8)	1
371	79	96	(+17)	92	86	(− 6)	83	91	(+ 8)	5
323	91	100	(+ 9)	97	103	(+ 6)	93	101	(+ 8)	1
242	76	76	(0)	59	65	(+ 6)	64	70	(+ 6)	1
318	76	81	(+ 5)	94	104	(+10)	84	90	(+ 6)	1
203	112	127	(+15)	124	117	(− 7)	119	124	(+ 5)	2
188	102	110	(+ 8)	104	101	(− 3)	103	106	(+ 3)	1
79	108	109	(+ 1)	98	110	(+ 2)	107	110	(+ 3)	7
276	91	91	(0)	93	97	(+ 4)	91	93	(+ 2)	1
351	71	64	(− 7)	53	62	(+ 9)	59	61	(+ 2)	2
104	89	92	(+ 3)	82	80	(− 2)	85	86	(+ 1)	5
194	94	99	(+ 5)	108	105	(− 3)	101	102	(+ 1)	1
238	70	67	(− 3)	76	80	(+ 4)	70	71	(+ 1)	1

Seizures controlled: 12 (60.0%), Improved: 5 (25.0%), Same or worse: 3 (15.0%)

more points, two were seizure free (9.5%). This correspondence is not nearly as pronounced if one looks at the improved or same/worse group. This finding reemphasizes, therefore, the value of long-term follow-up studies. It points out also that insistence on complete control of seizures (i.e. no seizures at all within the limits of the follow-up period, not just a decrease in frequency of occurrence) is not only theoretically desirable, but

of very practical importance. It would be advisable when follow-up results for epileptic patients are reported in the future, that the time interval between last seizure and follow-up date be clearly and explicitly stated. This has not been done in a considerable proportion of reported studies. Looking at the figures presented in Tables 101-103 in reverse, we find that out of eighteen patients who were seizure free for two years or more the IQ had increased in twelve (66.6%), stayed the same or decreased

TABLE 102

RELATIONSHIP OF IQ CHANGE TO SEIZURE STATE AT FOLLOW-UP: NO CHANGE IN IQ, OR MILD DECREASE UP TO SIX POINTS

Patient Number	*Verbal*			*Performance*			*Full Scale*			*Seizure State*
	I	*II*		*I*	*II*		*I*	*II*		
236	95	96	(+ 1)	93	92	(− 2)	94	94	(0)	4
287	73	78	(+ 5)	90	84	(− 6)	80	80	(0)	8
395	85	89	(+ 4)	99	96	(− 3)	91	91	(0)	5
370	59	65	(+ 6)	103	95	(− 8)	78	77	(−1)	4
157	95	93	(− 2)	89	89	(0)	92	91	(−1)	4
225	94	87	(− 7)	73	73	(0)	82	80	(−2)	3
379	84	84	(0)	106	100	(− 6)	94	90	(−4)	4
347	69	69	(0)	77	69	(− 8)	71	67	(−4)	3
219	110	110	(0)	102	93	(− 9)	101	97	(−4)	4
77	82	84	(+ 2)	105	93	(−12)	92	87	(−5)	1
86	102	98	(− 4)	89	83	(− 6)	96	91	(−5)	1
139	121	114	(− 7)	114	115	(+ 1)	121	115	(−6)	1
150	101	95	(− 6)	104	98	(− 6)	103	97	(−6)	7
250	113	111	(− 2)	99	88	(−11)	107	101	(−6)	3
367	97	85	(−12)	90	92	(+ 2)	93	87	(−6)	1

Seizures controlled: 4 (26.6%), Improved: 8 (53.3%), Same or worse: 3 (20.0%)

slightly in four (27.7%), and decreased seven or more points in two (11.1%). When we look at the amount of increase or decrease in regard to the seizure state, we find that only one patient had deteriorated clinically and gained by three IQ points. There are two patients who were seizure free for two years, but lost eleven and eight points respectively. While freedom from seizures does not therefore guarantee an unchanged or improved IQ, a substantial increase in IQ in the presence of continued seizures appears quite unlikely.

TABLE 103

RELATIONSHIP OF IQ CHANGE TO SEIZURE STATE AT FOLLOW-UP: MODERATE TO MARKED DECREASE IN IQ POINTS

Patient Number	*Verbal*			*Performance*			*Full Scale*			*Seizure State*
	I	*II*		*I*	*II*		*I*	*II*		
338	101	95	(− 6)	121	115	(− 6)	111	104	(− 7)	7
266	87	79	(− 8)	89	82	(− 7)	87	80	(− 7)	2
100	96	90	(− 6)	110	106	(− 4)	104	97	(− 7)	4
118	110	108	(− 2)	99	90	(− 9)	107	100	(− 7)	4
177	110	106	(− 4)	102	95	(− 7)	109	102	(− 7)	3
322	73	67	(− 6)	80	69	(−11)	74	66	(− 8)	2
801	114	107	(− 7)	113	108	(− 5)	116	108	(− 8)	1
365	99	92	(− 7)	108	100	(− 8)	104	95	(− 9)	7
383	102	100	(− 2)	101	84	(−17)	102	93	(− 9)	7
277	101	93	(− 8)	92	80	(−12)	96	87	(− 9)	4
346	104	94	(−10)	108	102	(− 6)	107	97	(−10)	3
399	91	89	(− 2)	109	95	(−14)	101	91	(−10)	3
294	117	109	(− 8)	119	106	(−13)	119	108	(−11)	1
240	119	118	(− 1)	112	88	(−24)	117	105	(−12)	2
196	121	111	(−10)	118	108	(−10)	123	110	(−13)	3
168	84	72	(−12)	81	67	(−14)	81	68	(−13)	3
53	113	103	(−10)	118	108	(−10)	118	105	(−13)	7
381	103	95	(− 8)	112	96	(−16)	108	95	(−13)	4
145	122	104	(−18)	108	98	(−10)	118	102	(−16)	5
158	103	90	(−13)	104	77	(−24)	104	84	(−20)	4
285	84	71	(−13)	100	69	(−31)	91	68	(−23)	5

Seizures controlled: 2 (9.5%), Improved: 14 (66.6%), Same or worse: 5 (23.8%)

TABLE 104

CODE FOR THE NUMBERS UNDER SEIZURE STATE AT FOLLOW-UP EXAMINATION

1 Seizure free for 2 years or more
2 Practically seizure free except for occasional auras
3 Somewhat improved
4 Slightly improved
5 Same
6 Slightly worse
7 Somewhat worse
8 Moderately worse
9 Markedly worse

Concentrating on the actual IQ values, we can see that movement in the upward or downward direction can occur at any IQ level. The Verbal and Performance IQ tended to move for the most part in the same direction, but there were notable exceptions. In Case 283, the Verbal IQ increased by twenty points, but Performance IQ decreased by five points leading to a Full Scale increase of nine points. A similar situation occurred in Cases 371 and 203 and to a less marked extent in others. The opposite situation, a definite decrease in Verbal IQ coupled with a definitely increased Performance IQ, was observed only once (Case 351), although smaller fluctuations were seen in other cases (e.g. Cases 238 and 367).

We have stated before that the Performance IQ area tended to suffer more than the Verbal areas. It was therefore of interest to divide the patients on the basis of their Performance IQs in order to ascertain the characteristics of the individual whose Performance IQ is likely to deteriorate. It was hoped that this would bring the problem into sharper focus than exclusive reliance on Full Scale IQ. The fifty-six patients were divided into two groups: twenty-three patients whose Performance IQ had dropped by seven or more points, and thirty-three patients whose Performance IQ had decreased less, remained stable, or actually increased. The previously mentioned 190 variables were again used for analysis of variance and the statistically significant results for the F and Chi Square tests are shown in Tables 105 and 106. Duration of seizure disorder in regard to minor seizures heads the list. The group whose Performance IQ had dropped had, on the average, suffered from minor seizures for approximately ten years, while the other group had this condition for less than six years. Maximal frequency of major seizures as well as frequency at time of initial visit were significantly related to Performance IQ loss. The patients whose Performance IQ had decreased by seven or more points had, on the average, maximally one or more seizures per week and at time of initial evaluation, two to three per month. The other group had maximally two to three seizures per month and seven to twelve per year at time of first evaluation. The group that had lost Performance IQ points had also shown a poorer response to anticonvulsant treat-

ment, had more than one seizure type, and more frequently had clusters of major seizures over a few days. The patients were older on initial evaluation, had higher IQs to start with and less organic pathology on psychological testing. Unexpected were the observations that female patients more commonly tended to show loss of Performance IQ points, and so did patients whose seizures were classified as absences. It should be emphasized again that these patients did not necessarily suffer from "pure petit mal" with three cycles per second spike wave patterns in their EEGs, but that some of them had focal temporal EEG abnormalities, while the EEG was nonspecifically abnormal in others.

TABLE 105

INITIAL EXAMINATION FINDINGS RELATED TO SUBSEQUENT PERFORMANCE IQ SCORES

	PERFORMANCE IQ			
	Decreased 7 or more points (N = 23)	*Decreased less or remained same* (N = 33)	*F*	*Significance Level* (%)
Duration of seizure disorder for minor seizures	7.8	5.7	12.3	1
Frequency of major seizures at initial evaluation	6.8	4.5	11.2	1
Object Assembly—Wechsler IQ	11.5	8.8	9.3	1
Maximum frequency of major seizures	8.3	6.4	9.1	1
Block Design—Wechsler IQ	11.0	8.5	8.3	1
Age	23	17	7.7	1
Organic pathology suspected from psychological tests	2.0	3.8	7.4	1
Performance IQ—Wechsler IQ	102.6	90.9	7.2	1
Clusters of major seizures over several days, freedom from seizures for several weeks	2.4	1.3	6.4	5
Combination of seizures	2.7	1.9	5.7	5
Response to anticonvulsant medication for period of three months to one year after onset of illness	2.6	5.1	5.7	5
Full Scale IQ	101.1	90.6	5.6	5
Picture Arrangement—Wechsler IQ	10.6	8.6	5.5	5
Response to anticonvulsants after the first year of treatment	4.4	6.3	4.1	5

Family history of epilepsy was not significantly related to Performance IQ changes. The positive relationship with family history of abortions would require confirmation on another sample before it can be definitely accepted. The observation that psychiatric treatment had been recommended much more frequently in patients whose Performance IQ had subsequently shown a decrease is of interest in regard to our previously mentioned hypothesis that IQ fluctuations are likely to manifest themselves in emotional disturbances. It is conceivable that these

TABLE 106

INITIAL EXAMINATION FINDINGS RELATED TO SUBSEQUENT PERFORMANCE IQ SCORES

		Performance IQ			
		Decreased 7 or more points	*Decreased less or remained same*	X^2	*Significance Level* (C_C)
Psychiatric treatment suggested					
	Absent	14	31	7.4	1
	Present	9	2		
Family history of abortions					
	Absent	13	29	4.7	5
	Present	8	3		
Absence					
	Absent	13	28	4.1	5
	Present	10	5		
Male		9	23	3.9	5
Female		14	10		

patients had already experienced some IQ loss, even before initial evaluation which showed itself in behavioral symptomatology—which in turn was regarded as being of psychogenic origin. The total Performance IQ decrease may have been greater than is indicated by the two values that we obtained, because a pre-illness IQ was not available in these cases. A long-term study spanning at least ten years, starting at the time of the patient's first seizure with annual or biannual IQ tests, would be necessary to test this hypothesis.

Relationship of Intelligence to Age at Time of Onset of the Seizure Disorder

It has been mentioned in the chapter on seizure prognosis that a comparison was carried out between three groups of patients: those whose seizures had started between birth and three years of age, between four and twelve years of age, and thirteen to twenty-seven years of age. The statistically significant differences between these groups in regard to intellectual functions

TABLE 107

SIGNIFICANT DIFFERENCES IN INTELLECTUAL FUNCTIONS RELATED TO AGE AT ONSET OF THE SEIZURE DISORDER

	AGE AT ONSET				
	0–3 (N = 27)	*4–12* (N = 31)	*13–27* (N = 30)	*F*	*Significance Level* (%)
Object Assembly—Wechsler IQ	8.2	9.2	11.6	6.6	1
Talking age	5.4	4.2	3.4	5.2	1
Amount of schooling	2.8	4.0	4.3	5.2	1
Full Scale IQ	84.8	90.4	101.3	5.1	1
Verbal IQ	84.8	90.9	100.7	5.0	1
Digit Span—Wechsler IQ	6.4	8.0	9.6	3.9	5
Comprehension	7.6	9.1	10.4	3.3	5
Performance IQ	87.3	91.5	100.4	3.2	5
"Organic" Bender-Gestalt Test	5.0	3.7	2.9	3.1	5
				X^2	
Rotation of Bender Designs					
Absent	6	18	23	6.7	5
Present	8	10	5		

are shown in Table 107. It is immediately apparent that there are impressive relationships. The later the onset of the illness, the more normal the intellectual functions. One might assume that early onset also reflects longer duration of the illness, but this was not the case in this sample. Duration of illness prior to first evaluation was not different between the three groups. In contrast to what we have seen in the previous tables the Verbal areas rather than the Performance items (with exception of

Object Assembly) tended to be involved to a greater extent. We have seen before that deterioration as a result of the seizure disorder tended to affect the Performance area more than the Verbal tests. When it comes to intellectual development it would seem from this table that the Verbal areas are more afflicted than the Performance items. This particular aspect of the problem requires further study on another sample. The overall trend is, however, quite clear. The prognostic significance of a seizure disorder starting in early childhood lies in regard to the future intelligence of the patient, rather than in problems with seizure control. It could of course again be argued that children who develop seizures early in life are *a priori* brain damaged and the patient's IQ is lower, not because of seizures but because of underlying brain damage. While this is certainly the case in a number of instances, it is not the whole explanation because it was pointed out in a previous section that etiological factors did not show significant differences in regard to age at time of onset of the illness. Most clinicians will be familiar with cases of patients who developed normally until the seizure disorder made its appearance, but did not progress in a satisfactory manner thereafter. The cases of infantile spasms of unknown etiology present the most dramatic example. Doctor West's child is well worth remembering in this connection: "The child is now a year old, was a remarkably fine healthy child when born and continued to thrive until he was four months old. It was at this time that I first observed slight bobbings of the head forward . . . ."

This case is so important because the father, being a physician, would have been readily aware of birth injury, congenital malformation, or acute inflammatory disease of the central nervous system.

Discriminant Function Analysis

In spite of the fact that we had only a small sample of patients with two Wechsler IQ scores, an attempt was made to use discriminant function analysis in order to try to predict the patient whose IQ is likely to deteriorate. As had been mentioned in the chapter on seizure prognosis, complete data on each

variable was required for the computer program, and this led to a further decrease in the number of patients who became available for this aspect of the study. Group I consisted of nineteen patients whose IQs had dropped seven or more points, and Group II of twenty-nine patients whose IQs had dropped less, had remained essentially the same, or had increased by any number of points. Seven variables that had shown the largest differences between the two groups were chosen for the discriminant function analysis. Eighteen of the nineteen patients of Group I (i.e. had lost more than seven IQ points) were correctly classified by this procedure (95.0%), and so were twenty-

TABLE 108

DISCRIMINANT FUNCTION FOR PREDICTING LOSS OF 7 OR MORE IQ POINTS

Variables	WEIGHTS *Discriminant Function I*	*Discriminant Function II*
Combination of seizures	5.85	4.99
Frequency of major seizures at present	−1.60	−1.53
Clusters of seizures for several days, freedom from seizures for several weeks	3.01	2.19
EEG background amplitude	2.92	3.20
Organic pathology suspected from psychological tests	9.22	9.79
Social factors contributing to illness	4.01	3.42
Full Scale IQ	0.99	0.93
Constant	−79.22	−71.88

four patients of Group II (83.0%). The variables involved, as well as the weights and constants for the discriminant function, are shown in Table 108. Table 109 shows the probabilities indicated by the computer classification in relation to actual findings.

The coding of the variables "combination of seizures," "organic pathology suspected from psychological tests," and "social factors contributing to illness" has already been mentioned in previous chapters. EEG background was coded as shown in Figure 19 and for Full Scale IQ the actual score was inserted. Frequency of seizures refers to major seizures only. If the patient did not have major seizures, the variable was coded as 1

TABLE 109

PROBABILITIES FOR PATIENTS TO FALL INTO GROUP I OR GROUP II

	Correct Classification	*Incorrect Classification*
*Group I**		
Less than .75	4	0
.75 to .89	9	1
.90 to .95	5	0
*Group II***		
Less than .75	7	2
.75 to .89	7	3
.90 to .99	10	0

* IQ decreased 7 or more points.

** IQ decreased less than 7 points, remained the same, or increased.

BACKGROUND RHYTHMS VOLTAGE

0 Not recorded
1 0–10 μv
2 10–20
3 20–30
4 30–40
5 40–50
6 50–60
7 60–70
8 70–80
9 Above 80

FIGURE 19.

(frequency less than once a year) because a score of zero would have meant missing data and this was not acceptable for the computer program. An example of a patient who is likely to show loss of seven or more IQ points might be as follows:

EXAMPLE—POOR PROGNOSIS FOR INTELLECT

DISCRIMINANT FUNCTION I:

VARIABLE NAME	*WEIGHT*	*CODE AND DEFINITION*	*RESULT*
Combination of seizures	5.85 × 3	Two seizure types	17.55
Clusters of seizures over a few days, freedom from seizures for several weeks	3.01 × 2	Rarely	6.02

EEG background amplitude	2.92 × 3 20–30 μv	8.70	
Organic pathology suspected from psychological tests	9.22 × 2 Mild	18.44	
Social factors contributing to illness	4.01 × 2 Mild	8.02	
IQ	0.99 × 118	116.82	
	SUBTOTAL	175.55	
Frequency of major seizures at present	−1.60 × 9 Several a week		−14.40
CONSTANT	−79.22		−79.22
	SUBTOTAL		−93.62
	TOTAL	81.93	

DISCRIMINANT FUNCTION I (175.55 minus 93.62 = 81.93)

DISCRIMINANT FUNCTION II:

Combination of seizures	4.99 × 3 Two seizure types	14.97	
Clusters of seizures over a few days, freedom from seizures for several weeks	2.19 × 2 Rarely	4.38	
EEG background amplitude	3.20 × 3 20–30 μv	9.60	
Organic pathology suspected from psychological tests	9.79 × 2 Mild	19.58	
Social factors contributing to illness	3.42 × 2 Rarely	6.84	
IQ	0.93 × 118	109.74	
	SUBTOTAL	165.11	
Frequency of major seizures at present	−1.53 × 9 Several a week		−13.77
CONSTANT	−71.88		−71.88
	SUBTOTAL		−85.65
	TOTAL	79.46	

DISCRIMINANT FUNCTION II (165.11 minus 85.65 = 79.46)
Discriminant Function I (81.93) minus Discriminant Function II (79.46) = 2.47
The probability of the patient falling into Group I (i.e. suffer loss of seven or more I.Q. points) is .92.

The results obtained by the discriminant function analysis suggest that prognostication in regard to intellectual deterioration may very well be possible, but the weights were developed on a small sample of patients, and the study should be repeated on a larger population. It should also be mentioned that these weights were derived from an adolescent and adult population and are therefore not necessarily applicable to children. Patients with childhood epilepsy present a special problem in this respect. In the child one could visualize the existence of two separate processes; both would result in progressively lower IQ scores, but they would have different origins. One process would be arrest or slowing of mental growth, and the other an actual loss of previously acquired material. It is conceivable that a number of children with epilepsy whose IQ scores decrease over the years do not, in fact, suffer at that time from a deteriorating process, as the progressively lower IQ scores would suggest; but their mental growth curve may be flattened and their abilities are being measured against increasing chronological age, leading to progressively lower scores. An example might illustrate this point.

A seven-year-old boy was recently seen at the Michigan Epilepsy Center for reevaluation. At the time of initial evaluation he had suffered from psychomotor seizures and his Full Scale IQ was reported as 90. Seizures had stopped thereafter, but he was returned to the Center for reevaluation because of a learning problem in school. His IQ two years later was measured as 73. Using the weights of the discriminant function analysis, the formula predicted that the patient would fall into Group II (i.e. loss of six points or less, or actual gain in IQ points), with .75 probability on the basis of the information obtained at inital evaluation. This was, of course, in contrast to the actual finding because the patient had "lost" seventeen points and he should have been placed into Group I (i.e. loss of seven or more points). On the basis of the previous assumption that one may be dealing in certain cases not with actual deterioration but with arrest or slowing of development, the patient's current achievement on the IQ test was rescaled. This time we did not use his actual chronological age of seven years, but his previous age of five

years. This resulted in an IQ level of 98, or an eight-point increase over his previous achievement. This finding indicates that if the patient had been an adult, the formula would have classified him correctly, and we are dealing here not with deterioration from a higher level to a lower level, but merely with a markedly slower growth curve. This aspect of prognosticating intellectual achievements in children will require further detailed study.

The formula also does not take into account those few cases of epileptic patients who suffer from what has been termed "petit mal status" or "spike wave status." An IQ obtained during a period of marked cerebral electrical abnormality may be spuriously low and increase by ten or more points within a few days if the patient's EEG clears up spontaneously or as a result of change in anticonvulsant medication. "Petit mal status" may not always be so pronounced that it can be easily diagnosed clinically, and the correct diagnosis rests entirely upon the electroencephalogram. Two examples might serve as illustrations:

Example 1. Patient P. M. was, at the time of initial evaluation, a ten-year old boy who had suffered from a febrile convulsion at ages three, five and seven respectively. Subsequently, he developed afebrile seizures recurring every six months until the age of nine. Grand mal seizures became exceedingly frequent thereafter; he had approximately one seizure a day, and he also had one episode of status epilepticus. He was placed on Dilantin and had no further major seizures, but numerous minor attacks occurred during which the eyes rolled up and the head jerked backwards. These occurred at the rate of approximately twelve a day. There was a family history of convulsive seizures, his seven-year-old brother had febrile convulsions, the paternal grandfather had suffered from epilepsy, and one paternal cousin also had seizures in childhood. On clinical examination the child was somewhat confused and slightly disoriented, but the rest of the neurological examination was normal. The Wechsler intelligence scales were as follows: Verbal, 75; Performance, 74; and Full Scale, 72. His electroencephalogram is shown in Figure 20. It shows repeated episodes of high voltage spike wave activity lasting four to five seconds at a time and recurring every ten to fifteen seconds. For practical purposes the EEG showed nearly continuous seizure activity, but there were no obvious clinical manifestations in the patient. After having tried several anticonvulsant drugs without success in the hospital, the patient received Librium®

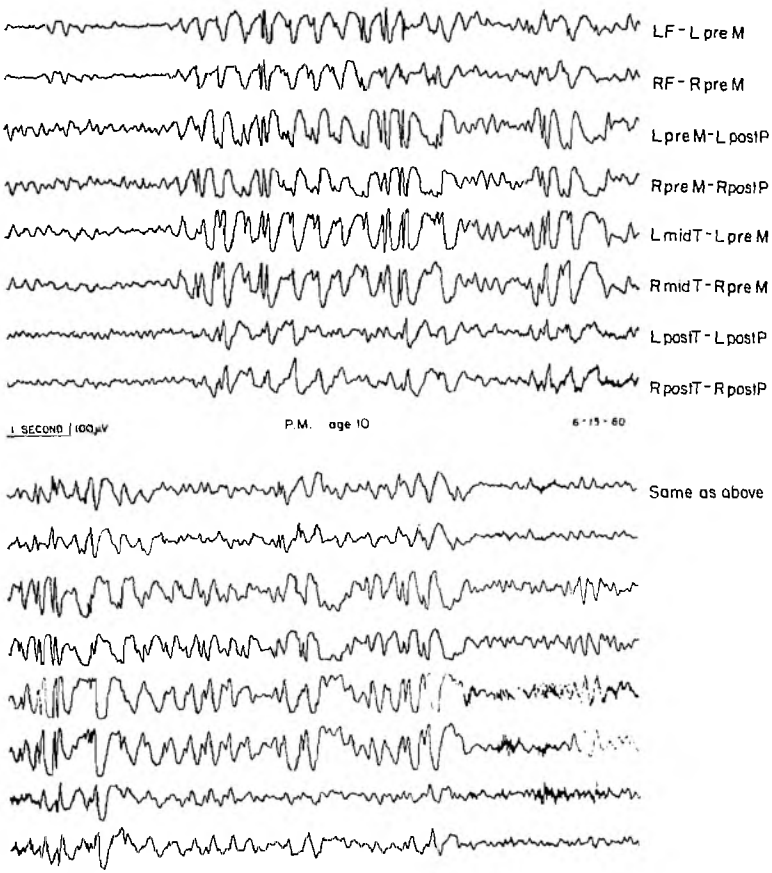


FIGURE 20. High voltage diffuse 2-3 c/s spike wave activity lasting several seconds, repeating every 10-15 seconds. Verbal IQ 75, Performance IQ 74, Full Scale IQ 72.

and this abolished the seizure activity in the EEG. The record showed a completely normal appearance during the waking state as shown in Figure 21, although there were still brief episodes of spike wave activity during sleep. The IQ, taken three days after the patient's EEG had shown marked improvement, was measured: Verbal, 90; Performance, 101; and Full Scale, 95. A reevaluation of the patient in 1966 showed the waking record still normal and during sleep there were some diffuse bursts but no appreciable spike components. The patient has not had any grand mal seizures in the meantime, although he did occasionally have some staring episodes. His Verbal IQ was 98; Performance IQ, 107; and Full Scale IQ, 102.

While this patient could have been regarded as a case of

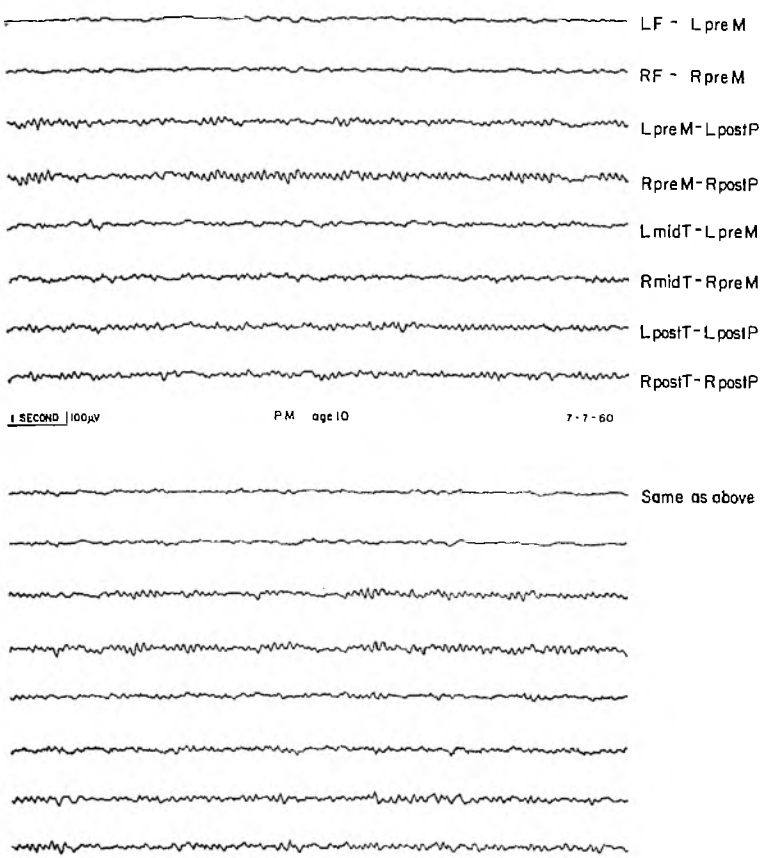


FIGURE 21. Record was obtained three weeks after that shown in Figure 20. Verbal IQ 90, Performance IQ 101, Full Scale IQ 95. Rather dramatic increase especially of Performance IQ.

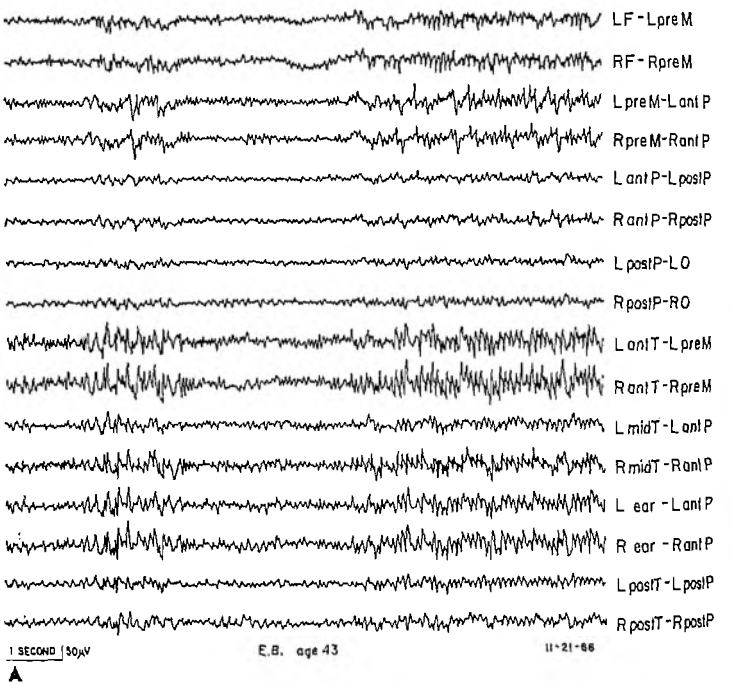
"petit mal status" or "spike wave status," patient E. B. presented a considerably different electroencephalographic picture but rather similar clinical findings.

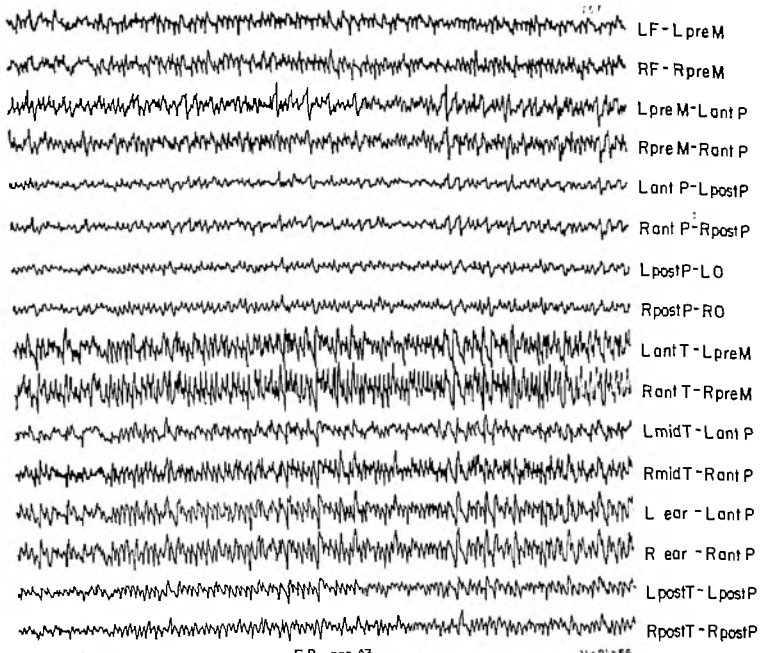
Example 2. Patient E. B. was a forty-three-year-old male, when seen in 1966, and since the age of two had suffered from nonfocal grand mal seizures which usually recurred once a year. From 1957 to 1965 he had a complete remission. Seizures recurred in 1965 after the death of his mother. He was then placed on Mesantoin® (200 mg four times a day) and had no major seizures thereafter, but he developed prolonged episodes lasting several days during which he is restless, confused, and unable to sleep. This state decreases after two or three days and the patient is mentally alert

without any difficulties for three or four days and then the cycle repeats again. An example of the patient's EEG is shown in Figures 22 A, B, C, D, and E. His IQ was obtained on a day when his electroencephalogram showed this marked disturbance, and it was recorded as a Verbal IQ of 98; Performance IQ, 71, and Full Scale IQ, 86. His IQ on a day when the electroencephalogram was essentially normal, as shown in Figures 23 A and B, was Verbal IQ, 104; Performance IQ, 84, and Full Scale IQ, 95.

It was felt that this patient was on inordinate amounts of medication and it was decreased to Mesantoin® (100 mg four times a day), phenobarbital (65 mg three times a day), and Eskabarb® (100 mg at bedtime). This led to a marked improvement in the patient's condition. He had no major seizures and a marked decrease in frequency of occurrence as well as in length of the confusional states.

These cases clearly illustrate the value of the electroencephalogram in assessing the various causes of a patient's intellectual dysfunction. Due to the fluctuating nature of their disorder, epileptic patients lend themselves in a unique way to the study of mind-brain relationships, and the data that we have obtained so far are presented in the hope that they may stimulate further interdisciplinary investigations between psychologists, neurologists and electroencephalographers.




LF - L preM
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L postP - LO
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L ant T - L preM
R ant T - R preM
L mid T - L ant P
R mid T - R ant P
L ear - L ant P
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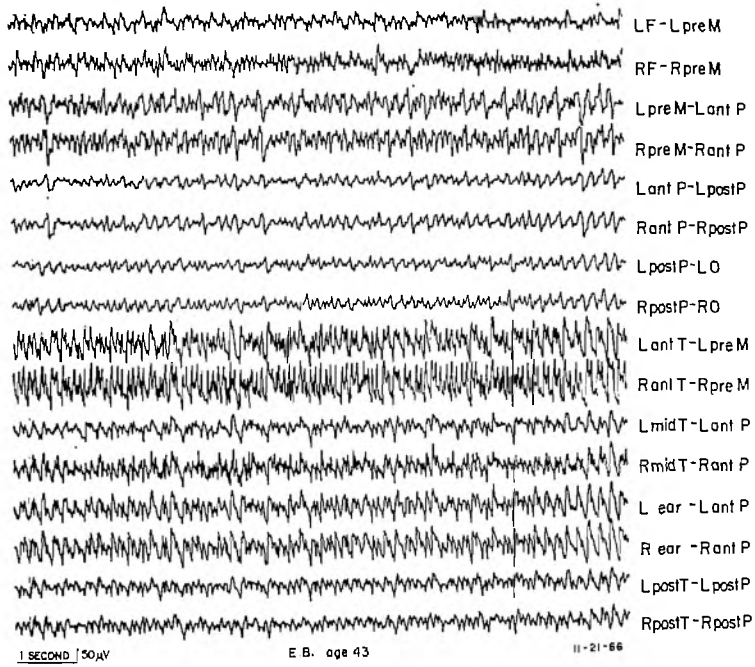
1 SECOND 50μV
E.B. age 43
11-21-66

B


LF - L preM
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L ant T - L preM
R ant T - R preM
L mid T - L ant P
R mid T - R ant P
L ear - L ant P
R ear - R ant P
L postT - L postP
R postT - R postP
1 SECOND 50μV
E B. age 43
11-21-66

C

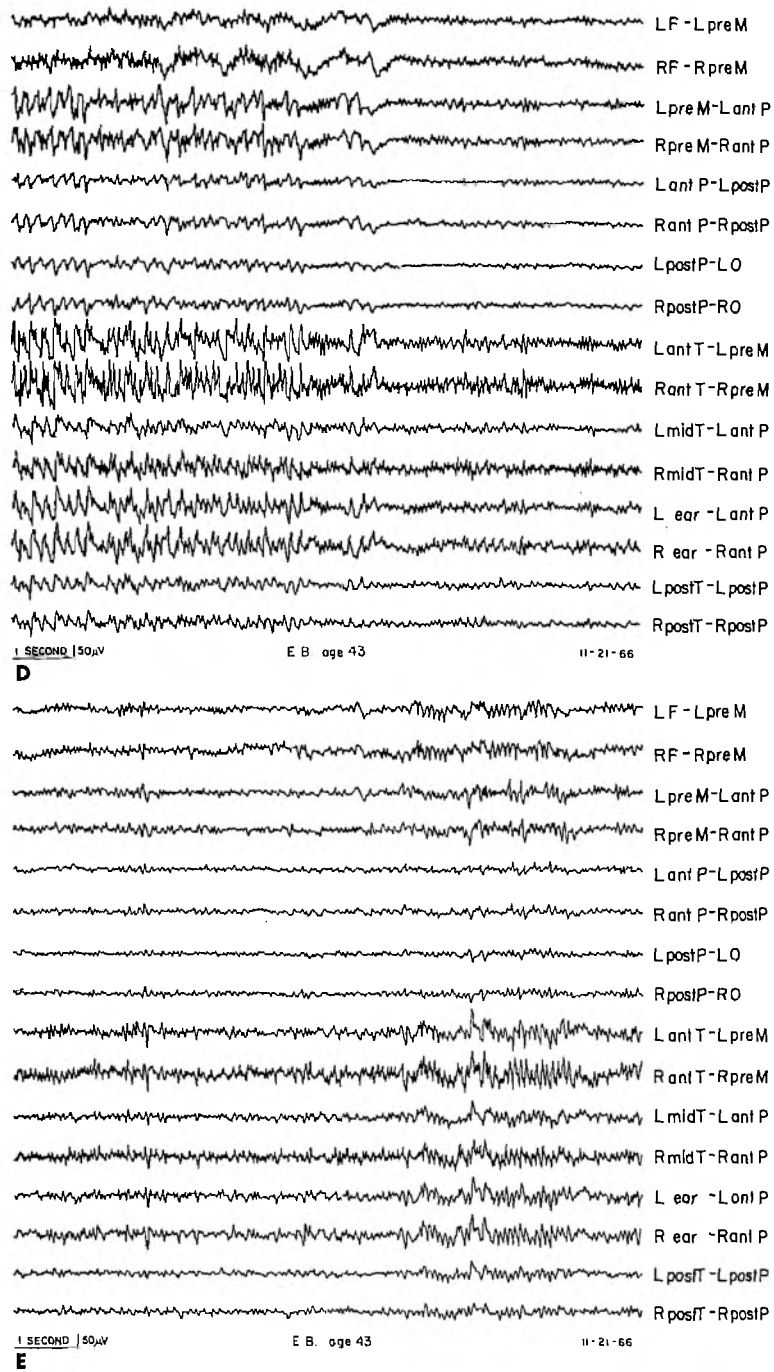

FIGURE 22. A-E represent 50 consecutive seconds of recording. Episodic high voltage diffuse spike activity most pronounced in anterior head regions lasting between 2 and 25 seconds, recurring every 5-15 seconds. Verbal IQ 98, Performance IQ 71, Full Scale IQ 86.

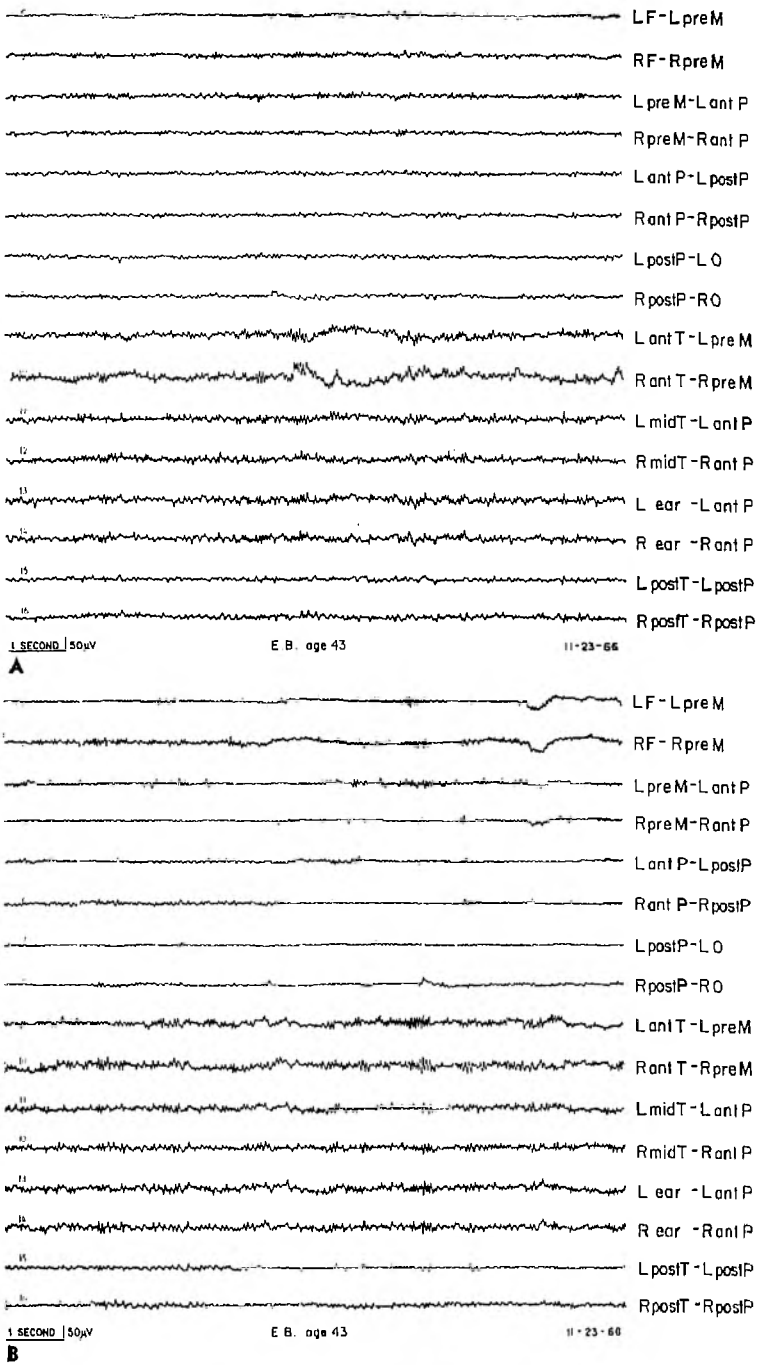

FIGURE 23. A and B represent 20 consecutive seconds of recording. Tracing was obtained two days after that shown in Figure 22. EEG somewhat disorganized but no seizure patterns. Verbal IQ 104, Performance IQ 84, Full Scale IQ 95. Further example that Performance IQ is more interefered with by seizure activity than Verbal IQ.